

***United States Court of Appeals
for the
District of Columbia Circuit***



**TRANSCRIPT OF
RECORD**

BRIEF AND APPENDIX
FOR APPELLANT

IN THE

United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA

—
No. 7893
—

CANADIAN-AMERICAN PHARMACEUTICAL
COMPANY, *Appellant*

v.

CONWAY P. COE, *Appellee*

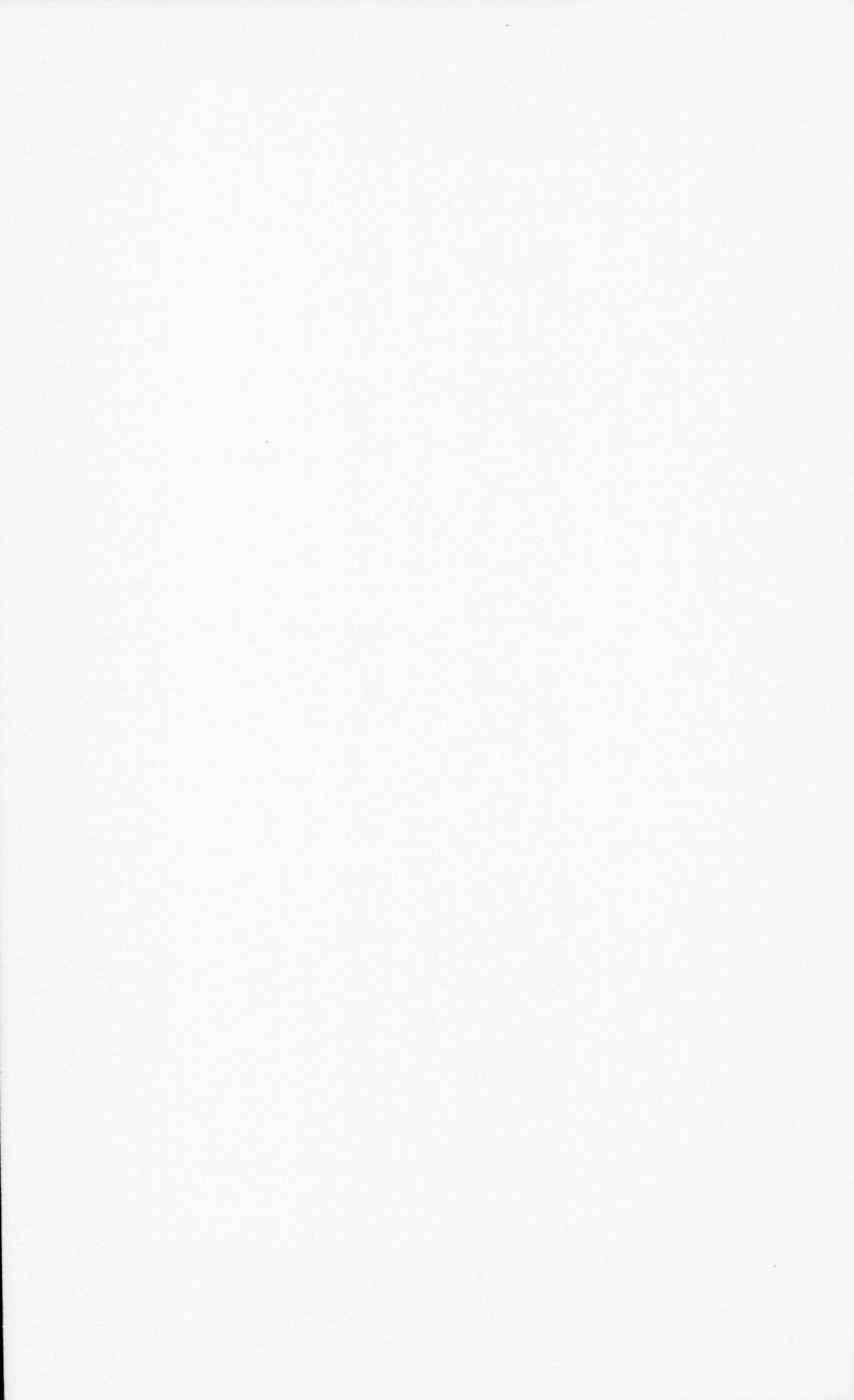
Appeal from the District Court of the United States for the
District of Columbia.

ARTHUR G. CONNOLLY
Counsel

Address: Arthur G. Connolly
Wilmington, Delaware

JAMES P. BURNS
Counsel

Address: James P. Burns
807 Munsey Bldg.
Washington, D. C.



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**Appeal from the District Court of the United States for the
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BRIEF FOR APPELLANT.

I. JURISDICTIONAL STATEMENT.

This court has jurisdiction of the present appeal because it was taken from a final judgment of the District Court of the United States for the District of Columbia, rendered in a suit brought by plaintiff-appellant* under Section 4915 of the Revised Statutes (U.S.C., Title 35, Sec. 63), against defendant, a resident of the District of Columbia. (App. 1 and 2)**

*Plaintiff-appellant will hereafter be referred to as plaintiff, and defendant-appellee will hereafter be referred to as defendant.

**App. when used herein designates appellant's appendix.

II. STATEMENT OF THE CASE.

The appeal seeks reversal of a judgment dismissing plaintiff's complaint filed under Section 4915 of the Revised Statutes.

The invention in question is defined by claims 2, 3, 4, and 6 to 12, inclusive, of U. S. Patent Application Serial No. 137,931, entitled "New Pain-Alleviating Material", filed in the United States Patent Office April 20, 1937. (Plaintiff's Ex. No. 1) The claims are set out in the complaint (App. 3 and 4) The invention pertains to a product, referred to for convenience as "Ensol", capable of reducing the pain resulting from cancer, and processes for its manufacture.

The District Court found as a fact that "The prior art does not disclose or anticipate either the process or the product", and that "there is no evidence that plaintiff's product causes any harmful effects". (Findings of Fact Nos. 3 and 4; App. 179)

Since the process and product claims are patentably novel, the sole question to be decided is whether the invention is possessed of sufficient utility to justify the issuance of a patent under Section 4893 of the Revised Statutes. As conceded by defendant's counsel in the opening sentence of his closing argument before the District Court, "* * *, our sole argument here is as to utility." (Tr. 149)

On this question of utility, the District Court has found as a fact that the testimony of plaintiff's witnesses and certain of the exhibits was to the effect that the invention had reduced pain due to cancer in approximately 65 per cent of the cancer patients treated therewith. (Findings of Fact No. 5; App. 179)

Plaintiff's uncontradicted and unchallenged testimony and documentary evidence is based upon more than five years of intensive research and clinical investigation by many able physicians on over seventeen hundred people suffering from cancer. Yet, this positive proof has been held to be overshadowed by four papers describing alleged negative laboratory experiments on a small number of animals (primarily mice) which were completed in a matter of

weeks. This, despite the fact that the sole question in issue concerned pain reduction and skilled experts testified, and it is not denied, that pain reduction could not be determined by animal experiments. This, despite the fact that independent medical experts of the Ontario Government, after extended investigation, unhesitatingly acknowledged the outstanding utility of the invention. This, despite the fact that the Ontario Government, which gave Insulin to the world, is supporting this work and defraying the cost of producing and shipping this product throughout the world for the relief of cancer patients and was so interested in this invention that it permitted two of its representatives to testify in support of the invention in the court below.

The question of reducing pain in cancer patients, particularly those in the last stages of the disease, is of extreme importance. Next to heart trouble, more people die from cancer each year than from any other cause. Furthermore, the number of people dying from cancer is on the increase.

In the face of these facts, which are beyond dispute, let us see what has been done about the disease. Today, the cause of cancer remains unknown. Today, cancer is practically incurable after it has metastasized, *i. e.*, developed secondary growths. Today, the great majority of patients suffer indescribable pain in the last stages of the disease. Today, with the exception of the present invention, the only method of reducing pain in the advanced stages of cancer is the use of opiates such as morphine. Today, opiates are admittedly unsatisfactory because they are habit-forming, must be given in constantly increasing doses, produce in the patient a tolerance which finally defeats their purpose, and because they act to temporarily deaden and paralyze the brain. These facts established in the record are, however, so well known that they are practically matters for judicial notice.

Less progress has been made in the cancer field than in any other important field of medicine. The Government of Ontario, which gave Insulin to the world, appreciated this appalling situation. It appointed an official commission to

investigate new discoveries in the cancer field and to encourage those which its investigation proved to have merit.

This commission has carefully investigated the present invention over a period of more than a year. As a result of this investigation, it has unhesitatingly acknowledged the utility of this invention. In fact, the Ontario Government was so positive that this invention was of value in the treatment of cancer that it assumed the entire expense of producing this product and shipping it throughout the world for use in the treatment of cancer patients.

Any more complete acknowledgment of utility would be hard to find than that of a foresighted government which considers an invention to be so important to humanity that it bears the total expense of manufacturing and shipping it to physicians in every part of the world.

The two representatives of the Ontario Government who directed the laboratory and the clinical investigation of this invention have testified in the court below. These men are well known and highly respected physicians who have devoted many years to the study of cancer. They speak as unbiased representatives of the Ontario Government. It is their considered opinion that this invention is of definite value in the reduction of pain due to cancer. They have, likewise, testified that this invention is a valuable contribution to the medical practitioner. (App. 58 and 66)

In addition to the official representatives of the Ontario Government the following witnesses have testified that this invention possesses pronounced utility in the alleviation of pain due to cancer:

Dr. Robert N. Irwin, a practicing physician who has used the invention on his cancer patients over a period of several years.

Dr. James C. Connell, father of the inventor and Dean of the Queen's Medical School for more than 25 years.—This testimony was on written interrogatories as Dr. Connell was in such poor health that he was unable to travel.

The inventor, a practicing physician of many years' experience.

The documentary exhibits are by physicians of integrity and wide experience. They point indisputably to the value of this invention in the reduction of pain due to cancer. These documents describe investigations carried on by their authors over a period of years on many patients in the last stages of cancer. The investigations were conducted not only in Canada but also in the United States and even as far away as Australia.

Arrayed against the testimony and documentary exhibits just referred to are the four notes or papers describing experiments conducted for brief periods on a small number of animals. Attention is particularly directed to the fact that these publications are concerned solely with the regression of transplanted animal tumors. In no instance do they deal with spontaneous cancer tumors such as are encountered in human beings. They do not mention or throw any light on the question of pain alleviation. In fact, pain alleviation cannot possibly be determined by animal experiments. (App. 58 and 67)

III. THE STATUTE INVOLVED.

The court below based its decision upon Section 4893 of the Revised Statutes (U.S.C., Title 35, Sec. 36), which is in the following words:

“On the filing of any such application and the payment of the fees required by law the Commissioner of Patents shall cause an examination to be made of the alleged new invention or discovery; and if on such examination it shall appear that the claimant is justly entitled to a patent under the law, and that the same is sufficiently useful and important, the Commissioner shall issue a patent therefor.”

As previously mentioned, the single question to be decided is whether the invention is sufficiently useful to justify the issuance of a patent under the above statute.

IV STATEMENT OF POINTS.

Plaintiff intends to rely upon the following points wherein it believes the court below was in error:

1. In not holding that the invention defined by claims 2, 3, 4, 6, 7, 8, 9, 10, 11, and 12 of United States patent application Serial No. 137,931 is sufficiently useful and important to warrant the grant of a patent thereon;
2. In not holding that the articles by Gye, Pommerenke, Goldfeder and Rusch & Preston were irrelevant to a determination of the issue of utility;
3. In not holding that the testimony of plaintiff's witnesses proved that the invention in issue was sufficiently useful and important to warrant the grant of a patent thereon;
4. In not holding that plaintiff's exhibits proved that the invention in issue was sufficiently useful and important to warrant the grant of a patent thereon;
5. In holding that the subject matter of the claims in issue is not possessed of sufficient utility to justify the issuance of a patent under Section 4893 R.S. (U.S.C., Title 35, sec. 36);
6. In holding that plaintiff is not entitled to a patent containing claims 2, 3, 4, 6, 7, 8, 9, 10, 11, and 12;
7. In entering judgment in favor of the defendant and dismissing the complaint herein.

V. SUMMARY OF ARGUMENT.

Plaintiff's argument is divided into a number of parts concerned with the following propositions:

1. **The pleadings admit the degree of utility required by the decisions.** The defendant admitted in paragraph 10 of his answer that the Examiner had found that the claimed invention "when applied on certain cases possessed the property of reducing pain." He admitted in paragraph 12 of his answer that the Board of Appeals had found that "the relief of pain is noted in many of the cases." (App. 8)

While he denies the ultimate conclusion to be drawn from these admissions, *i. e.*, utility, his denial is ineffective as the facts admitted speak for themselves.

2. The references relied on to negative utility are irrelevant. The only evidence relied upon by the District Court to negative utility is contained in four papers published shortly after this invention was first made, over five years ago. These papers are by Gye, Rusch & Preston, Pommerenke, and Goldfeder. They describe nothing but animal experiments conducted solely in respect to transplanted tumors for the purpose of determining regression of animal cancer—not pain reduction.

It is conceded that none of the papers is concerned with pain reduction. Furthermore, plaintiff's experts have testified that even if one wished to, it would be impossible to determine pain reduction by tests on animals. There is no way to ascertain whether an animal is suffering pain from cancer, much less whether pain is increased or decreased under treatment. (App. 28, 58 and 67)

These papers, therefore, are irrelevant to the only point in issue.

3. The testimony proves that the invention is of outstanding value. The witnesses have testified that the invention was administered to more than a thousand patients by many physicians over a period of five years. In more than ninety per cent of the cases wherein pain was a symptom, this pain was reduced or entirely eliminated by means of this product. When one considers that more than 75 per cent of cancer patients experience pain, this benefit is indeed of great magnitude. Furthermore, in not a single instance was a patient harmed by this product.

This invention filled a great need on the part of the general practitioner. For the first time he was able to relieve patients in the last stages of cancer with a harmless, effective, and non-habit-forming product.

It would be hard to find a greater contribution to the art. Indeed there was a crying need for such a product over an

extended period of time. Many unsuccessful attempts have been made to satisfy the need, and finally the present invention which solves the problem has been enthusiastically endorsed by many skilled and unbiased physicians throughout the civilized world.

4. The documentary exhibits prove that the invention is of outstanding merit. Plaintiff's documentary exhibits comprise publications of the Hendry Connell Research Foundation; publications of general practitioners and cancer specialists who used this invention in treating their private cancer cases over a period of years; and a reprint of an address delivered by a medical specialist before a national meeting of the American College of Proctology.

These exhibits describe the extensive investigation devoted to ascertaining the value of the present invention in the treatment of cancer. The phenomenon of pain relief was obtained so consistently, in such a large number of cases, over such an extended period of time, and by so many skilled doctors working independently that no reasonable person would question it.

These exhibits describe other beneficial results in addition to pain reduction. These additional benefits do not detract from the value of the invention, as defendant appears to contend, but rather enhance it. It would be a strange rule indeed which penalized an invention because it was better than described.

Any inference which the defendant seeks to create by the failure of some case histories to refer to pain reduction is likewise unwarranted and unfair. Not all cases of cancer suffer pain so histories of these cases would obviously not refer to pain reduction.

5. The granting of a patent does not constitute approval by the United States of the invention. The defendant has stated that the granting of a patent would in effect constitute approval of this invention by the United States Government. (Tr. 39) This idea was erroneously entertained by the Patent Office, and it is believed that the court below

fell into the same error. The granting of a patent merely means that the invention is regarded as a patentable one—not that its use is recommended or endorsed by the Government.

It is believed that this unfounded assumption has probably contributed more to the adverse decisions below than any other factor. For that reason the court's attention is respectfully and urgently directed to the palpable unsoundness of the contention.

The present product is a serum, and as such it is subject to the U. S. Public Health Service Act of July 1, 1902, 32 Stat. 729, U.S.C. Title 42, sec. 145. Before a serum, patented or unpatented, can be sold, its place of manufacture, whether here or abroad, must be inspected and approved by the U. S. Public Health Service; the materials which go into its manufacture must be similarly approved; the personnel who manufacture it must be similarly approved; the containers in which it is shipped and the labels used must be similarly approved; the manner of shipping it must be similarly approved; its effectiveness in treating the public must be similarly approved. After all those approvals are obtained, a license is issued permitting its sale. *Not until then does it bear the stamp of approval of the Government.*

It is likely that no product sold in this country is as carefully controlled as a product in this category. That the issuance of a patent is tantamount to government approval of the use of the invention is, therefore, ridiculous and unworthy of serious consideration.

6. The independent investigation of the Ontario Government proves that the invention is of outstanding utility. When the late Sir Frederick Banting was an unknown medical doctor, his research was supported and encouraged by the Ontario Government. The result was Insulin, an immortal contribution to medicine.

It is significant that the Ontario Government also interested itself in the present invention. First, it had this invention carefully investigated by its own representatives,

with complete laboratory and clinical assistance which it placed at their disposal. As a result of this investigation, the representatives of the Ontario Government concluded that this invention reduced pain, was entirely harmless, and was of considerable value in the treatment of cancer.

Then the Ontario Government assumed the expense of producing this product and distributing it free of charge to physicians throughout the world. Each month more than ten thousand cubic centimeters of this product are produced at the expense of the Ontario Government and shipped to physicians as far away as Australia for use on their cancer patients.

Two official representatives of the Ontario Government who directed the investigation of this product testified in the court below. In their capacity as government representatives, they testified that they spent more than a year investigating this product from both the laboratory and the clinical standpoint. (App. 55-56; 64-65) They testified that they personally examined more than seventeen hundred cancer patients and case histories of cancer patients who had been treated with this invention. They testified that this investigation convinced them that the invention reduced pain due to cancer, that the invention was harmless, and that it was a valuable contribution to the medical practitioner. (App. 58 and 66) They testified that in addition to the property of reducing pain it had other valuable properties. (App. 57 and 66)

7. The medical practitioner is in great need of a harmless pain alleviant for cancer. From the dawn of civilization until the present time it is probable that less has been achieved for the cancer patient than for sufferers from any other disease. This is due partly to the complexity of the field and partly to the unreasoning opposition which is hurled at one who throws any light on it.

For more than ten years after they were found to be of value in the treatment of cancer, X-ray and radium were bitterly opposed and criticized, not only by the public but by leaders of the medical profession. (App. 12 and 13)

What is the result of this unreasoning opposition? The need for a simple and speedy diagnosis of cancer, for a harmless means of alleviating pain, for a cure, for a preventative becomes ever more desperate. Those who are in the last stages of cancer suffer and are penalized. Those who have cancer but don't know it, and there are many, are penalized as are also those who may some day become its victims.

This invention is an important contribution to one phase of the problem—relief of pain. It is not claimed as a cure. It may also be an important contribution to other phases of the problem. This fact cannot negative its established merit. That such a contribution to humanity is worthy of patent protection should be self-evident.

8. The evidence on behalf of plaintiff completely outweighs that of defendant.

In support of plaintiff's case is the testimony of five witnesses, all medical doctors of high standing, excellent training, and wide experience in the field of cancer. In addition there are many publications describing the remarkable effectiveness of this invention in reducing the pain due to cancer. This affirmative evidence is based upon more than five years' intensive investigation of over a thousand human cancer patients, most of whom were in the last stages of the disease.

In support of defendant's case are four papers describing animal experiments conducted for the sole purpose of determining regressions of transplanted tumors. Not one of these experimental reports refers to pain reduction. Not one of them has any bearing on the question of pain reduction. Not one describes a test made on a single human being, the only way that pain reduction can be determined. (App. 26, 58 and 67)

VI. ARGUMENT.

1. The Pleadings Admit the Degree of Utility Required by the Decisions.

The law in this case is well settled. It is to the effect that an invention possesses utility if it will accomplish its stated objective at all, even though it may be crude and imperfect.

Hildreth v. Mastoras, 257 U. S. 27, 34; 66 L. Ed. 112, 116
Telephone Cases, 126 U. S. 535; 31 L. Ed. 989

Since the utility of an invention is seldom attacked there are relatively few decisions on this point. These decisions are, however, by courts of outstanding competency. They are clearly to the effect that the test of utility is of a much lower order than that of commercial success or technical perfection. Accomplishment of the desired objective to any extent whatsoever is sufficient.

Seymour v. Osborne, 78 U. S. 516; 20 L. Ed. 33
Mergenthaler Linotype Co. v. Press Pub. Co., 57 Fed. 502, 505
Lamb Knit Goods Co. v. Lamb Glove & Mitten Co. et al., 120 Fed. 267, 272
Callison v. Dean et al., 70 F. 2d. 55, 58
International Tooth Crown Co. v. Hanks Dental Association, 111 Fed. 916
Gibbs v. Hoefner, 19 Fed. 323, 324
Walker on Patents, (Deller's Ed., 1937), page 310 *et seq.*

The opinion in *International Tooth Crown Co. v. Hanks Dental Association*, *supra*, is of considerable interest in this connection because it was rendered by an eminent patent jurist, Judge Lacombe, and involved a charge to a jury in a patent infringement action where lack of utility was the principal defense. As jury trials are a rarity in patent infringement suits Judge Lacombe took particular pains to make his charge as complete and illuminating as possible. It is:

"If there is any utility in it, (the invention), that is sufficient to support the patent. The measure of utility does not make any difference. It would be a perfectly valid patent if a device is a useful one, although 50 or 100 others might be very much more useful, and although improvements upon the device might make it more useful than it was before. Nor is it necessary that a continuation of usefulness be shown or that it must be for a long period of time. That is not essential. If it is useful at all, it sufficiently meets the requirements of the statute that the invention must be a new and useful one to warrant the granting of a patent."

It is submitted that the law on this question of utility, when applied to the facts admitted by the pleadings would compel a decree for plaintiff, even in the absence of any evidence whatsoever.

That portion of paragraph 10 of the complaint which is admitted by the defendant is as follows:

10. That on information and belief the Examiner specifically acknowledged that "it appears * * * from a careful inspection of the case as filed that the material resulting from the process when applied in certain cases possessed the property of reducing pain." (App. 4)

That portion of paragraph 12 of the complaint admitted by the defendant is as follows:

12. That said invention, on appeal from the action of the Examiner, was further passed upon by the Board of Appeals who stated inter alia that:

"While the relief of pain is noted in many cases, this feature is usually not particularly stressed * * *." (App. 5)

The pleadings, therefore, admitted that the claimed invention "when applied in certain cases possessed the property of reducing pain" and that "the relief of pain is noted in many of the cases." While the defendant denied the ultimate conclusions to be drawn from these facts, *i. e.*,

utility; his denial is a nullity. Utility is a question of fact, and the facts admitted by defendant conform to the test for utility laid down by the courts. Nothing more is required.

The defendant begs the issue when he argues that reduction of pain does not take place in a sufficiently large percentage of cases, or that it is not particularly stressed in the case histories. Such contentions have no bearing on the issue of utility. It appears that defendant is endeavoring to evaluate the utility of an invention by applying to it tests for commercial success. This is improper. The adoption of such a test by the tribunals below, we submit, constituted reversible error.

2. The References Relied on to Negative Utility Are Irrelevant.

The sole issue concerns the question of whether or not the claimed invention possesses the degree of utility required by the patent laws. All the evidence relied upon by the defendant to negative utility comprises four items: a note by Gye, a paper by Rusch & Preston, a paper by Pommerenke, and a brief note by Goldfeder. (Defendant's Ex. 1-B to 1-E inclusive, App. 148 to 168)

These papers relate to certain animal experiments carried on with products, allegedly the same as that in issue, on mice or rabbits having transplanted tumors, for the purpose of determining tumor regression. Attention is respectfully directed to the fact that the objective of *each* of these experiments was to determine tumor regression—not pain reduction. Attention is also respectfully directed to the fact that each of these experiments was performed on a small number of animals for only a brief period of time in the very early period of plaintiff's development. The record clearly shows that these animal experiments were not and could not be of value in a determination of pain reduction. (App. 26, 58 and 67) Attention is likewise respectfully directed to the fact that we have nothing but the unsupported word of the individual authors, who were unavail-

able for cross-examination, that the product which was used was identical with the invention here in suit.

It is submitted that these articles dealing with brief experiments on animals having transplanted tumors are utterly devoid of any dependable evidentiary value in deciding the issue of this case. Such tests cannot be relied upon to support any reliable conclusions. Most important of all, the question of pain reduction was not attempted and could not have been determined by tests confined to animals not even suffering from spontaneous cancer.

The following excerpts from the record, it is believed, prove the complete irrelevancy of these publications:

Dr. Walter T. Connell (no relation to the inventor), a physician and official representative of the Ontario Government, who had independently investigated the clinical properties of this invention for more than a year and a half, testified on this point as follows:

Q. Doctor, do you believe it is possible to determine the pain reducing properties of a product by an investigation conducted on rats, mice, rabbits, or other animals?

A. I do not know any way we can estimate pain sensed by these animals or to register whether or not they get relief. (App. 58)

Dr. Eugene P. Johns, a physician and official representative of the Ontario Government, who had independently investigated this invention in the laboratory for more than a year and a half, testified on this point as follows: (App. 66 *et seq.*)

Q. Dr. Johns, do you believe that a determination of the pain reducing properties of a product might be ascertained by means of tests on animals?

A. I do not think that you can determine pain relief in animals. I think that you are probably referring to tumors in animals, and during the course of the last 10 or 12 years I have seen probably thousands of spontaneous and transplantable tumors in animals, and I

know of no way that you can tell whether the presence of that tumor is causing pain in the animal.

These animals will have tumors. They get pretty large. I have seen tumors whose bulk would be perhaps more than the whole of the animal when the tumor is removed, and yet these animals with the tumors will be running around in the cage with the rest of the normal mice apparently enjoying themselves, eating, drinking, carrying on, carrying on apparently a normal mouse existence.

They cannot talk to you.

The only method of estimating it is by subjective symptoms, and I have never seen any subjective symptoms which would lead you to believe that they did not have pain or that there might be any relief from pain.

Q. Are you familiar with the published articles of Gye, Rusch & Preston, Pommerenke, and Goldfeder, referred to in the defendant's answer and I believe in evidence as defendant's Exhibits B, C, D, and E?

A. Yes, sir. One of the first things that was necessary when we started this investigation was to review the literature which had accumulated with regard to the use of Ensol and which was confirmatory or otherwise.

Q. Did these articles have any bearing on the question of pain reduction in cancer?

A. I do not see where they have any bearing on that question at all, sir.

As I have said, I do not know of any way in which you can assess pain in animals and how these experiments would be of value in that connection I just cannot see it, sir.

Q. What, if any, conclusions have you as to the value of these articles individually and collectively in determining the efficacy of this invention in the treatment of cancer?

A. We, when we commenced this work, of course we had to take into consideration, as I say, other published articles, and we had to assess them at their—as to what we considered their meaning in regard to our own research. I do not feel that they have very much bearing on the problems that we have to undertake. The reason for that statement was that, there were probably several, the most important probably was the fact that we had available to us a large number of clinical rec-

ords present in the files of the Foundation; there were approximately 1700 or 1800 of these records; they were collected from a cross-section of the country by some hundreds of physicians and our review of these records definitely indicated that in at least two-thirds of the cases definite advantages were gained by the use of Ensol including, of course, relief from pain.

Those cases were the experiments, the human experiments, if you will. *They were conducted on humans, on humans who were suffering from spontaneous tumors, tumors which arose in the individual; many of them were in cases who had exhausted any recognized or other method of therapy, including surgery, X-ray and radium and, as I say, they did show very definite benefits.*

On the other hand, you have *the investigation by Gye, Pommerenke, Rusch & Preston, and Goldfeder, who were working on animals and whose results were essentially negative according to their conclusions.*

Personally, we prefer to believe the evidence which was given by a large number of investigators on a large series of cases rather than the evidence presented by four investigators on a comparatively small series of animals. (Italics ours)

* * *

Q. Does that answer apply to all four of these articles, Doctor?

A. Yes. According to my recollection *all of these articles were done on transplantable tumors in animals, mice, rats, and rabbits.*

I do not think—I am quite sure none of them used spontaneous tumors and, of course, there is a difference between a spontaneous tumor and a transplantable tumor.

The spontaneous tumor is one which arises in the individual who has the cancer; it rises from his own cells. The transplantable tumor is one which arises or may have arisen years back in some other animal and has been transferred through successive generations and some of those tumors at the present time are 10 or 15 years old, transferred through susceptible animals, and the original tumor being 10 or 15 years old. (App. 70) (Italics ours)

Dr. James C. Connell, father of the inventor, Dean Emeritus of Queen's Medical School, testified on this point as follows:

Int. No. 42. Is the pain alleviating property of a product customarily determined by treating patients with it?

A. Yes, such tests can only be made by the use on patients. Animal experimentation can never elucidate pain relief. The suffering patient is the last court of appeal and the physician accepts his verdict as to the results which follow the use of any remedy.

Cross-Int. No. 90. State in detail your reasons for your answer to Cross-Interrogatory No. 89?

A. The work of Rusch & Preston, Pommerenke, Gye, and Goldfeder in connection with the product of the application in suit is of no value for the following reasons,—

1. No part of their work dealt with pain relief which is the basis of this application.

2. Their experimental work was conducted upon mice. Pain relief cannot be proven by animal experimentation. No clinical work was undertaken by any of these investigators although opportunity was afforded them to do so.

* * *

5. There is no evidence that the product employed by these men was similar to that of the product in question.

6. Experiments reported by these men were completed within a few weeks. It is obvious that their work was superficial and inadequate, * * *.

7. In the case of Gye, some months after he published his reports in 1935, his assistant wrote to ask how the solution was produced. * * *

* * *

9. There is no reference in any of these publications to pain alleviation.

* * *

Red.-Int. No. 91. Did the publications of any of the individuals referred to in Cross-Interrogatory No. 88

pertain either directly or indirectly to a determination of pain alleviation?

A. No.

Red.-Int. No. 92. State your reasons for your answer to the preceding interrogatory.

A. No reference can be found in any of the publications in question to pain relief or to the clinical use of the product. Pain relief can only be determined by clinical use of the product in question or of any other substance by clinical use upon human patients who are suffering pain. No clinical use was reported by any of the investigators mentioned in Cross-Interrogatory No. 88. It is absolutely impossible to learn anything about pain control or relief by tests upon animals. (App. 26 to 28)

Four reputable physicians who have been intimately associated with this product over a period of years have testified that the animal experiment reports relied upon to negative utility are of no conceivable value for this purpose. They have stated that it is impossible to determine pain reduction by means of animal experimentation. Furthermore, these articles do not even attempt to determine pain reduction, but deal with an entirely different subject,—tumor regression. It is, therefore, submitted that defendant's Exhibits 1-B to 1-E inclusive, should be ignored as irrelevant in their entirety and that the tribunals below committed error in predicated their decisions thereon.

3. The Testimony Proves that the Invention is of Outstanding Utility.

(a) The inventor.

Q. In approximately what percentage of the cancer patients, suffering pain and treated with Ensol and with whom you are acquainted, was this pain reduced as a result of this Ensol treatment?

A. Approximately 90%, between 90 and 96%, I believe. (App. 35)

(b) The Ontario government representative.

Q. Approximately how many patients and case histories of patients treated with this invention have you investigated?

A. Slightly over 1700.

Q. Based upon your investigation of those cancer patients treated with Ensol, Doctor, have you any conclusions as to the approximate percentage of those cases which experienced reduction in pain as a result of this treatment?

A. * * * Now in the investigation of these case histories it was found that about roughly 65% did show relief, pain relief. * * * (App. 56 & 57)

Q. As a result of this investigation, Doctor, and the number of years you have been interested in this subject, is it your opinion that this product which alleviates or reduces pain in approximately 65% of cancer cases treated is a valuable contribution to the medical practitioner?

A. I consider it as such as a result of my investigation.

Q. Would you or would you not as a result of this investigation recommend the use of this product in conjunction with X-ray, radium, or surgery in the treatment of cancer patients?

A. As the material has proven itself to be harmless and as it has certain effects in alleviating symptoms, reducing pain, increasing well-being, prolonging life, I certainly would consider it advisable to use it.

Q. Would you recommend Ensol for those purposes, Doctor, if you had any doubt as to its harmlessness?

A. I certainly would not if I thought it in any way harmful. If I thought it in any way harmful I would not recommend its use.

Q. Would you recommend Ensol for this purpose if you had any doubt as to its efficacy?

A. No, I certainly would not recommend it if I had. (App. 58)

(c) A private practitioner.

Q. How many of your cancer patients have you treated with Ensol?

A. I have treated with Ensol 18 cancer patients.

Q. In approximately what percentage of those patients was pain a symptom?

A. I would say of the 18 pain was definitely a symptom in 14.

* * *

Q. In what percentage of the 14 who had pain as a symptom was there a reduction in this pain due to Ensol treatment?

A. Definitely in 12.

Q. In the treatment of your cancer cases with Ensol, have you ever noticed any harmful effects?

A. I have not. (App. 80)

Q. Were you enabled by means of this Ensol treatment to reduce the amount of opiates they were receiving?

A. I can definitely say I have reduced opiates to the point where they were discontinued entirely, and I recall patients that were reduced from $1\frac{1}{2}$ grains of morphine a day, where you could tide them along with nothing but aspirin and keep that up until death, and opiates and heavy sedatives were not required in that period. (App. 82)

Q. Over what period of time were you able to reduce this pain in these patients by means of Ensol administration?

A. If you get a reduction of pain, that reduction will remain until that patient either expires or, if they continue to improve, they still have pain reduction.

Q. Did the pain disappear entirely in any of these patients under Ensol administration?

A. Definitely yes.

Q. Do you know of any other means of accomplishing comparable results?

A. I do not. (App. 83)

(d) Inventor's father and Dean Emeritus of Queen's Medical School.

Int. No. 20. How many doctors have administered this product in the treatment of their cancer patients?

A. Impossible to give the exact number. It is, however, in excess of one thousand. (App. 15)

* * *

Int. No. 23. What is the consensus of opinion of these physicians as to the pain alleviating properties of this product, based upon the case histories which you have received from them and examined?

A. The almost unanimous opinion of these physicians is that the use of this product alleviated the pain in cancer. It also produced other beneficial effects and no harmful reactions have ever been observed or reported. (App. 23-24)

Int. No. 30. Approximately what percentage of cancer patients, wherein pain is a symptom, have experienced alleviation of pain by the use of this product?

A. Above 90%.

Int. No. 31. Upon what do you base your answer to the last question?

A. My answer is based upon a personal study of the case histories of 382 cases of cancer in relation to pain. Of these 24% had no pain or pain was so slight in character that medication for its relief was not required. 289 cases required drugs in some form for the relief of pain. These 289 cases were treated with this product and in 279 or 96%, pain was partially or completely relieved.

This study has been published and the percentages have not been questioned. (App. 16)

4. The Documentary Exhibits Prove that the Invention is of Outstanding Utility.

(a) **Plaintiff's Exhibit No. 4** is a publication of the Hendry Connell Research Foundation. On pages 126 and 127 is an article dealing with the specific phenomenon of pain in malignant disease. The second paragraph of this article succinctly outlines the effectiveness of the invention here in suit in reducing pain due to cancer. It is as follows:

"The other 289 cases required drugs in some form for relief of pain. All these received Ensol treatment and in 279 or 96%, pain was partially or completely relieved. While a much larger group should be studied to give accurate percentages it can be said that approximately 76% of cases of malignant disease require medication for the relief of pain. Further it appears that 73% of all cases treated with Ensol were relieved of pain in some degree." (App. 96)

(b) Plaintiff's Exhibit No. 5 is an article on the treatment of cancer with Ensol. This article was written by Dr. Neville Davis, a surgeon of Sydney, Australia. Dr. Davis has practiced surgery in Sydney for more than twenty years. He is on the staff of one of the leading Australian hospitals and was formerly a staff member of the Mayo Hospital in Rochester, Minn. He bases his article on the information which he obtained by treating a group of his cancer patients with this product.

This information is summarized in the aforesaid exhibit as follows:

“Ensol injections do not cause patients any serious discomfort. On the contrary, even in extreme cases with ultimate death of the patient, it has been shown to give relief of pain, diminish the quantity of opiates used, improve appetite, increase weight, generally relieving distressing symptoms.” (Tr. 572)

(c) Plaintiff's Exhibit No. 6 is a reprint of an address before the American College of Proctology. The address was by Dr. Thomas F. McNamara, a proctological specialist located in Rochester, New York, and personally unknown to the inventor. He had been forwarded sufficient amounts of the product in suit for treatment of his private patients. His experience therewith is summarized in this article.

In describing a rectal carcinoma case which he had treated for more than two years with this product Dr. McNamara stated:

“ * * * Ensol was used from July 1936 to date. There has been marked general improvement, a 22 pound gain in weight maintained to the present time. * * * The pain symptom has been relieved and the patient has not been receiving any type of analgesic.” (App. 103)

In another case history described by Dr. McNamara he states:

“The pain, sloughing, bleeding, discontinued about two months after the treatment had begun.” (App. 104)

(d) **Plaintiff's Exhibit No. 7** is another reprint from the Journal of the American College of Proctology. The article in question was written by Dr. Glenn S. Burton and is entitled "Ensol as an Aid in the Treatment of Rectal Cancer." This article is based upon 90 cases of rectal cancer personally treated by Dr. Burton at the clinic of the Hendry Connell Research Foundation. Of this number there were 59 who were treated with the product of this invention for a period of from two months to three and a half years. On the question of pain reduction of these cases it is stated:

"Of the 59 cases of rectal cancer treated with Ensol over a period varying from two months to three and a half years there were 43 cases, or approximately 75% who received benefit as estimated by pain relief and symptomatic improvement. 16 cases were not benefited. It is to be remembered that all these cases had already received all that could be done for them by accepted methods of treatment." (App. 106)

(e) **Plaintiff's Exhibit No. 8** is an article entitled "Relief of Pain in Cancer by the Use of Ensol." This article was submitted to the Ontario Commission for the Investigation of Cancer Remedies, by the Hendry Connell Research Foundation, under date of May, 1940. It describes 152 case histories of patients in the last stages of cancer who suffered considerably from the disease. On the question of pain reduction by means of this invention the article states, in summary:

"About 75% of cases of malignant disease require medication for the relief of pain. Morphia and its derivatives are commonly used for the purpose.

"Clinical experience during the past five years has shown that about 90% of these cases with pain, can be partially or completely relieved by the use of Ensol. No explanation is advanced for this pain relief. As progress is made in the investigation the reason for pain relief may become apparent." (App. 107)

It should be noted that about 75 per cent of cancer patients suffer pain. The remaining 25 per cent do not suffer

pain until the very last. In view of this fact it is not surprising that many of the case histories fail to mention pain reduction. These patients were fortunate enough not to experience pain.

Axiomatic as this may seem, the defendant has endeavored to create an unfavorable impression by the absence of a reference to pain reduction in some of the case histories. This is as unfair as it is illogical.

The defendant has also endeavored to capitalize on the reference in many case histories to beneficial results in addition to pain relief. While pain reduction is the most noticeable benefit many other beneficial results have also been observed. This should enhance the value of the invention, but the defendant by some strange reasoning is trying to infer the converse.

5. The Granting of a Patent Does Not Constitute Approval by the United States of the Invention.

It is believed that underlying the adverse decision of the court below was the erroneous supposition that to grant a patent on this invention would constitute official approval thereof by the United States Government. Neither the Patent Office nor the court would, under such conditions, care to take the responsibility of recommending the use of this product in the reduction of pain due to cancer. It is clear that no layman should be placed in the position where he directly or indirectly recommended the use of any product in the treatment of a disease as serious as cancer.

Fortunately, it is unnecessary for any layman or laybody to take such a responsibility, contrary to the view expressed by the defendant's counsel in his opening statement to the court below:

“In medical cases perhaps we are a little more strict than we are in other cases, but I think rightly so, because if we do grant the patent we have, in effect, placed the seal of Government approval on the product * * * .” (Tr. 39)

As long ago as 1902 the Congress took special recognition of the need to regulate the sale of viruses, serums, toxins, and analogous products. Products of this type, to which the present invention belongs, have been more carefully controlled and regulated than any other type of food, drug, or medicine.

The Act in question is entitled "An Act to Regulate the Sale of Viruses, Serums, Toxins, and Analogous Products in the District of Columbia, to Regulate Interstate Traffic in Said Articles and for Other Purposes", 32 Stat. 729, (U. S. C., Title 42, Sec. 145).

The production and sale of these particular products was deemed by Congress to be so important that they were placed under the supervision of the Treasury Department and the U. S. Public Health Service, instead of being placed under the Department of Agriculture where foods and drugs generally are regulated. Under the provisions of this Act, and the regulations adopted pursuant thereto, the sale of these products is subjected to minute inspection and control from the first step in the manufacture thereof until they reach the ultimate consumer.

Before any product of this type is sold, it must be licensed by the Secretary of the Treasury after approval by the U. S. Public Health Service. Before such a license is granted, the laboratory where the product is manufactured, whether here or abroad, must be inspected and approved by the U. S. Public Health Service. The efficacy of the product for its intended use must likewise be approved. The personnel, as well as the manufacturing and shipping operations must also be approved by the Public Health Service.

Regardless of whether a patent is issued to cover this invention, its approval by the U. S. Public Health Department and the Secretary of the Treasury is essential before it can be commercialized. In the face of such meticulous control by the U. S. Public Health Department, it is ridiculous to assume that the patenting of a product of this nature constitutes approval thereof by the Government.

6. The Independent Investigation of the Ontario Government Proves that the Invention is of Outstanding Utility.

The utility of this invention has been investigated in the most minute detail by the Ontario Government. More than a year ago this Government appointed two skilled physicians, with years of experience in the cancer field, to investigate this invention and report on its utility.

One of these representatives was to direct the clinical phase of the investigation and the other was to direct the laboratory phase. This investigation was carried on at Government expense, independently of the Hendry Connell Research Foundation, with a full-time staff of six assistants, housed in the Ontario Government Building. (App. 64-65)

As a result of this investigation the representatives of the Ontario Government concluded that the invention reduced pain, was absolutely harmless, and was of definite value in the treatment of cancer. They were so convinced of its utility that they unqualifiedly endorsed it as a valuable contribution to the medical practitioner in the treatment of cancer. (App. 58 and 66)

The Ontario Government thereupon assumed the expense of producing this product and distributing it free of charge to physicians for use in the treatment of their cancer patients. (Interrogatory No. 60, App. 20 and 21) For more than a year the public-spirited Government of Ontario has publicly conceded the remarkable value of this invention by bearing the entire expense of its production and distribution to all parts of the world.

7. The Medical Practitioner is in Great Need of a Harmless Pain Alleviant for Cancer.

Although the contributions to the field of cancer have been pitifully few it is surprising to note that each of these was accompanied by the greatest opposition from within the medical profession. At the present time there are but three recognized treatments for cancer. They are surgery,

X-ray and radium. Although X-ray and radium are now universally recognized as two of the three methods of treating cancer the medical profession bitterly opposed this use for more than fifteen years after their efficacy had been proved. (Interrogatories Nos. 10 and 11, App. 12)

The reason for this is set out in the testimony as follows:

“What was the early attitude of the medical profession with respect to the use of X-ray and radium in the treatment of cancer?

A. At first skeptical and critical, then very slow to accept reports published as correct. Ridicule and abuse heaped upon the early advocates, retarded its use and deprived many victims of cancer of the benefits to which they were entitled.

Confirmation of this can be obtained by reference to the medical press of the period between 1895 and 1920.

The following quotation was written more than 10 years after it became known that radiation was of use to control malignant disease:

From the Memoirs of Sir Almeric Fitzroy.
Clerk of the Privy Council.

“I have been obtaining information for the Prime Minister on the subject of a Royal Commission on cancer. * * * The medical profession will hear of nothing but the surgical treatment of cancer, partly because of its traditional repugnance to the introduction of new methods and possibly owing to the enormous profits that accrue from operations for cancer.

“Jenner, Simpson, and to a lesser extent, Pasteur and Lister, have all in turn had to encounter the opposition of the Mandarins of the profession.”
(App. 12 and 13)

Before the present invention the medical practitioner had but one method of reducing the pain due to cancer. That was the administration of opiates, with all of their attendant disadvantages. It was well known that opiates gave only temporary relief by drugging the senses. It was well known that opiates were habit-forming and had disagreeable reactions. It was well known that the dosage of opiates had to

be increased steadily in order to keep the pain under control. It was well known that in many cases the patient built up such a tolerance and craving for the drug that it was impossible to administer a sufficient amount to deaden pain. This was particularly true of those cases in the last stages of the disease.

The great need of a harmless pain alleviant for cancer is practically a matter for judicial notice. The following testimony portrays the stark reality of this question:

(a) The inventor.

Q. Would you mind mentioning, Doctor, what procedure was used in controlling or reducing pain in cancer patients prior to this discovery?

A. The only method of control of pain was the use of sedatives, particularly morphia and its derivatives.

Morphia and its derivatives are, of course, habit-forming drugs.

Naturally one held off using morphia until it had to be used; then it was found very often a tolerance in the patient was developed and gradually higher and higher doses had to be given which is, really, not a very satisfactory method of control. (App. 36)

(b) Representative of the Ontario government.

Q. Prior to the discovery of Ensol, how did the physician combat pain in the treatment of cancer patients, particularly those beyond the help of X-ray, radium and surgery?

A. Well, we were left, if they were beyond treatment with surgery, X-ray, or radium, we were left to the use of sedatives particularly, of course, morphia and its like substances, morphia, heroin, codine, and so forth.

Q. Did the use of sedatives for this purpose have any disadvantages, Doctor?

A. In the majority of cases you simply have to increase the dose to get the effect. One creates a tolerance for these substances.

Furthermore, those drugs also have an effect other than that of pain relief. They have effects like upset

stomachs, give rise to constipation, and other features that are objectionable. But we have to use them sometimes for pain relief despite their objectionable features. (App. 57)

(c) A practicing physician.

Q. Is it your opinion that Ensol has been of benefit to these patients?

A. It is my well considered opinion that Ensol is a weapon that is being placed in the hands of the family doctor which will give him something to use on those patients which has been the greatest advance we have ever had from the medical practitioner's standpoint in the treatment of cancer.

Q. Approximately how many injections of Ensol have you made in the treatment of patients?

A. I have used between 850 and 950 injections of Ensol in the treatment of patients.

Q. Over what period of time?

A. That is from 1937 until the present. (App. 80)

Q. Do you, as a practicing physician, consider that a product which will reduce pain in approximately two-thirds of the cancer patients, is a valuable contribution to the medical profession?

A. A product that will reduce pain in two-thirds of the cancer sufferers is the most valuable addition to cancer therapy that the general practitioner has ever had. (App. 83)

(d) Inventor's father and Dean Emeritus of Queen's Medical School.

Int. No. 32—What has heretofore been the customary method of relieving pain due to cancer?

A. The use of morphia or its derivatives.

Int. No. 33—Is this method completely successful?

A. No, not in any case.

Int. No. 34—What are its disadvantages?

A. All the well known disadvantages and objections connected with the use of morphia, especially in chronic cases of pain. Gradually increasing doses are necessary to give relief, the relief afforded is transient, the systemic disturbances which result and the final failure to produce relief with enormous doses.

Int. No. 35—Are these disadvantages recognized and admitted by the medical profession?

A. Yes and as well known to the laity as to the medical profession.

Int. No. 36—Has the product described in the patent application previously referred to evidenced properties superior to the pain alleviants about which you have just testified?

A. Yes, decidedly so.

Int. No. 37—In what respects is this product superior to the pain alleviants about which you have just testified?

A. The product in question is not habit-forming; in many cases the relief is immediate and complete, there are no systemic disturbances and natural sleep is secured. There are also other beneficial results from the use of this product. Appetite improves, weight is increased and there is a general sense of well-being created. (App. 17)

The record clearly proves that the invention has met a tragic need for a harmless pain alleviant for cancer, particularly in the final stages of the disease. A group of able and experienced physicians, after thorough investigation, have testified that the invention satisfies such need.

8. Balance Sheet of the Evidence.

On one side of the ledger we have the following evidence proving that the invention reduces pain in the majority of cases and is a great contribution to the field of medical science:

1. The inventor, a practicing physician with more than twenty years' experience. His ability was recognized by the Canadian National Research Council, which supported the research leading up to the present invention. For the past five years he has devoted his undivided time to this invention.
2. Dr. Walter T. Connell, no relation to the inventor, a practicing physician for the past forty-seven years, offi-

cial representative of the Ontario Government in charge of the clinical investigation of this invention. He devoted more than a year to this investigation and personally examined more than seventeen hundred cases and case histories. He concludes that the invention reduces pain in at least sixty-five per cent of cancer patients.

3. Dr. Eugene P. Johns, a physician with more than fourteen years' teaching and public health experience, official representative of the Ontario Government in charge of the laboratory investigation of this invention. He devoted more than a year to this investigation directing a staff of skilled scientists. He confirms utility of the invention.
4. Dr. Robert N. Irwin, a practicing physician with more than fourteen years' experience. He has treated a series of his cancer patients with this invention since 1937 and regards it as a tremendous contribution to medicine.
5. Dr. James C. Connell, father of the inventor, Dean of Queen's University Medical School for more than twenty-five years. He has been identified with this invention for more than five years and has personally examined the reports on all the patients treated with this invention during that period.
6. Pages 126 and 127 of plaintiff's Exhibit No. 4 describe 289 cancer cases, showing that the invention diminished pain in 96 per cent of the cases wherein pain was a symptom. (App. 96)
7. Plaintiff's Exhibit No. 5 is a publication by Dr. Neville Davis of Sydney, Australia. Dr. Davis was formerly a member of the staff of the Mayo Hospital in Rochester, Minn. He has practiced surgery in Australia for more than twenty years. For more than three years he has been using this invention on a series of his cancer pa-

tients and this publication describes the effectiveness of the invention on a representative group of these patients.

8. Plaintiff's Exhibit No. 6 is a reprint of an address delivered by Dr. Thomas F. McNamara before a national meeting of the American College of Proctology, giving significant instances of pain relief. Dr. McNamara is a proctological specialist of Rochester, N. Y.
9. Plaintiff's Exhibit No. 7 is an article by Dr. Glenn S. Burton which appeared in the Journal of the American College of Proctology. Dr. Burton is a practicing physician who was formerly assistant clinical director of the Hendry Connell Research Foundation. In this article he describes 59 cases of rectal cancer treated with this invention over a period of from two months to three and a half years, showing remarkable effectiveness in the relief of pain.
10. Plaintiff's Exhibit No. 8 is a report submitted to the Ontario Commission for the Investigation of Cancer Remedies by the Hendry Connell Research Foundation. It describes 152 representative cancer cases treated with this invention uniformly disclosing its effectiveness in the relief of pain.

To offset the above evidence on behalf of plaintiff we have four papers relied on by the defendant and the court below:

1. Defendant's Exhibit 1-B is a note by W. E. Gye, written in 1935, describing an experiment on mice to determine whether the growth of transplanted tumors was checked. A small number of mice were treated and the experiment was completed in a few weeks.
2. Defendant's Exhibit 1-C is an article by Rusch and Preston describing an experiment on rats and mice inoculated with transplantable tumors. The same remarks apply as for Defendant's Ex. 1-B.

3. Defendant's Exhibit 1-D is an article by Pommerenke describing an experiment on rabbits inoculated with transplantable tumors. The same remarks apply as for Defendant's Ex. 1-B.
4. Defendant's Exhibit 1-E is a three sentence abstract of an article by one Goldfeder describing an experiment on mice. The same remarks apply as for Defendant's Ex. 1-B.

The defendant's negative proof is without bearing on the issue here because :

(a) The animal experiments were conducted on animals which had been inoculated with transplantable tumors and in no instance on a spontaneous tumor such as encountered in human beings.

(b) The experiments were conducted by investigators whose objective was solely to determine tumor regression—not pain reduction.

(c) The experiments were conducted almost at the outset of plaintiff's development without the benefit of plaintiff's cooperation or experience.

(d) The experiments were brief; the findings were uncertain even as to the point investigated, e. g., tumor regression; they were incapable of establishing any fact germane to pain reduction and are irrelevant on the single issue here.

Plaintiff's affirmative evidence extends over a period of five years and embraces investigations of practicing physicians, cancer specialists, and government representatives, on more than one thousand cancer patients. Defendant's negative evidence extends over a period of weeks and embraces the investigations of a few laboratory workers on a small number of rats, mice, or rabbits for the purpose of determining not pain reduction but effect on tumor growth.

VII. CONCLUSION.

The claimed invention is new. All statutory prerequisites to the grant of a patent have been complied with. The district court found the invention to be unanticipated by prior art.

If the invention is useful, plaintiff is entitled to a patent thereon. To be useful, an invention need merely accomplish its desired objective, even though in a crude and imperfect manner. The objective of this invention is the reduction of pain due to cancer.

The usefulness of this invention has been acknowledged by general practitioners, cancer specialists, and public health officials after complete and independent investigation. Not only is it useful within the meaning of the patent statutes, but it is an outstanding contribution to the art. People in the last stages of cancer have nothing to take its place and are in dire need of it. It not only accomplishes its desired objective but goes far beyond.

The judgment below should be reversed and a patent should be authorized to issue on this highly meritorious invention.

Respectfully submitted,

ARTHUR G. CONNOLLY

JAMES P. BURNS

Counsel for Plaintiff-Appellant.

APPENDIX

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IN THE
United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA

No. 7893

CANADIAN-AMERICAN PHARMACEUTICAL COM-
PANY, *Appellant*

v.

CONWAY P. COE, *Appellee*.

Appeal from the District Court of the United States for the
District of Columbia.

APPENDIX TO BRIEF FOR APPELLANT.

I.

PLEADINGS.

1 *A. Complaint Under R. S. 4915 to Enforce Issuance
of Letters Patent*

Plaintiff, Canadian-American Pharmaceutical Company,
praying for the relief sought herein, respectfully alleges:

1. That Plaintiff, Canadian-American Pharmaceutical
Company, is a corporation organized and existing under
and by virtue of the Laws of the State of Delaware, hav-
ing its principal place of business at 1007 Market Street,
in the City of Wilmington, County of New Castle, and State
of Delaware;

2. That Defendant, Conway P. Coe., Commissioner of Patents and/or his successors in office, is a citizen of the United States and, in his official capacity, a resident of the District of Columbia;

3. That this court has jurisdiction of the cause of action herein because of the residence of the Defendant in the District of Columbia and because this is a suit for relief under Section 4915 of the Revised Statutes (Section 2 63 of Title 35 of the Code of Laws of the United States of America) as amended;

4. That Hendry C. Connell, M.D., a subject of the King of Great Britain, a citizen of Canada, and a resident of Kingston, in the Province of Ontario, and Dominion of Canada, believing himself to be the first, sole and original inventor of "New Pain-Alleviating Material", having satisfactorily complied with all the requirements of law in such cases provided did duly apply to the Commissioner of Patents for a patent thereon on April 20, 1937;

5. That said application to the Commissioner of Patents for letters patent of the United States was in due form of law, and therein did properly disclose, particularly point out and distinctly claim the art, method, process, composition and product constituting the invention or discovery of said Hendry C. Connell, M.D., and that said application was given Serial No. 137,931 by the Commissioner of Patents;

6. That said Hendry C. Connell, M.D., duly presented and prosecuted his aforesaid application and claims before the said Commissioner of Patents and in the course of such prosecution clearly delimited and pointed out in the claims his aforesaid invention, as will more fully appear from the duly certified copy of said application and the proceedings thereon of which profert will be made to the court at the proper time;

7. That said application is directed to an invention which is cognizable at law and in equity as patentable under the laws of the United States and the Rules of the Patent Office;

3 8. That, on information and belief, said Hendry C. Connell, M. D., was, in accordance with the Patent Laws of the United States, entitled to a patent on claims 2, 3, 4, and 6 to 12, inclusive, of said application, which claims* are as follows:

Claim 2. A process for producing a substance capable of reducing the pain resulting from cancer which comprises growing a proteolytic micro-organism on cancer tissue for a sufficient period of time to at least partially decompose said cancer tissue and extracting therefrom the liquid products produced thereby.

Claim 3. A process for producing a substance capable of reducing the pain resulting from cancer which comprises growing *B. Histolyticus* on cancer tissue for a sufficient period of time to at least partially decompose said cancer tissue and extracting therefrom the liquid products produced thereby.

Claim 4. A process for producing a substance capable of reducing the pain resulting from carcinoma which comprises seeding human carcinoma tissue with *B. Histolyticus*, incubating the seeded culture medium for a sufficient period of time and under such conditions that the carcinoma tissue is almost completely destroyed, separating the liquid from the solid portion of the resulting incubation mass and sterilizing said liquid.

Claim 6. The product produced in accordance with the process defined in claim 2.

Claim 7. The product produced in accordance with the process defined in claim 3.

Claim 8. The product produced in accordance with the process defined in claim 4.

Claim 9. A process for producing a substance capable of reducing the pain resulting from cancer which comprises treating minced cancer tissue with saline solution in order to remove therefrom substantial amounts of soluble constituents, adding to the residual extracted tissue dextrose and saline solution, inoculating it with *B. Histolyticus*, incubating it under anaerobic conditions for a sufficient period

*Claims in suit.

of time to substantially destroy the tissue and permit the supernatant fluid to become substantially non-colloidal, then filtering and rendering sterile the so-produced solution.

4 *Claim 10.* A process for producing a substance capable of reducing the pain resulting from cancer which comprises treating minced cancer tissue with saline solution in order to remove therefrom substantial amounts of soluble constituents, acidifying the solution containing said soluble constituents, refluxing it, neutralizing it, dialyzing it, adding to the residual extracted tissue said dialysate, dextrose and saline solution, inoculating it with *B. Histolyticus*, incubating it under anaerobic conditions for a sufficient period of time to substantially destroy the tissue and permit the supernatant fluid to become substantially non-colloidal, then filtering and rendering sterile the so-produced solution.

Claim 11. The product produced in accordance with the process defined in claim 9.

Claim 12. The product produced in accordance with the process defined in claim 10.

9. That, on information and belief, the Examiner specifically acknowledged that

“It appears from an examination of the claims and the art of record that the process claimed is novel per se * * *,” thus conceding that claims 2, 3, 4, and 6 to 12, inclusive, are not rejected on the prior art.

10. That on information and belief the Examiner specifically acknowledged that

“It appears * * * from a careful inspection of the case as filed that the material resulting from the process when applied in certain cases possesses the property of reducing pain,”

thus conceding the effectiveness of the invention defined by claims 2, 3, 4, and 6 to 12, inclusive.

5 11. That on information and belief the Examiner nevertheless erroneously and repeatedly rejected said

claims 2, 3, 4, and 6 to 12, inclusive, of said application on the sole ground that the invention defined thereby does not present

“an invention of sufficient importance to justify the issuance of a patent therefor under the provisions of R. S. 4893,”

which rejection was erroneously made final on or about May 12, 1938.

12. That said invention, on appeal from the action of the Examiner, was further passed upon by the Board of Appeals who stated inter alia that

“While the relief of pain is noted in many of the cases, this feature is usually not particularly stressed . . . ,”

thus conceding that the applicant has submitted evidence establishing limited utility of the invention as defined in rejected claims 2, 3, 4, and 6 to 12, inclusive.

13. That on information and belief, the Board of Appeals further specifically acknowledged, in their decision dated June 5, 1939, that

“We have no substantial proof before us as to the reliability of prior art descriptions of cancer pain relieving materials. These materials are quite different from appellant’s and we do not consider that they have any important bearing on the question before us,”

thus conceding the absence of prior art as a basis for its refusal to allow claims 2, 3, 4, and 6 to 12, inclusive.

6 14. That nevertheless the Board of Appeals rendered a decision dated June 5, 1939, on the appeal theretofore properly taken on claims 2, 3, 4, and 6 to 12, inclusive, erroneously affirming the decision of the Examiner, all of which will more fully appear from the duly certified copy of said application and the proceedings thereon of which profert will be made to the Court at the proper time.

15. That no appeal from the aforesaid decision of the Board of Appeals has been taken to the Court of Customs and Patent Appeals;

16. That the aforesaid patent application and all patents issuing thereon were properly assigned in their entirety to plaintiff, by a written instrument duly executed by said Hendry C. Connell, M.D., on January 17, 1938, and duly recorded in the United States Patent Office on October 31, 1939 (Liber H-181 Page 285); and that Plaintiff is now possessed of the entire right, title and interest in and to said application and patents;

17. That, on information and belief, the Commissioner of Patents has refused and still refuses to grant Letters Patent upon the aforesaid application for the invention embraced in rejected claims 2, 3, 4, and 6 to 12, inclusive, thereof, although Plaintiff is lawfully entitled thereto;

Wherefore, Plaintiff prays that this Honorable Court shall adjudge that the Plaintiff is entitled to have said claims 2, 3, 4, and 6 to 12, inclusive, allowed in said application

Serial No. 137,931, and shall authorize the said Defendant, Commissioner of Patents, to issue to the Plaintiff a patent on said application containing said claims on the filing in the Patent Office of a copy of this Court's adjudication and otherwise complying with the requirements of law; and for such other and further relief as the nature of the case may require and to this Honorable Court shall seem meet.

CANADIAN-AMERICAN PHARMACEUTICAL
COMPANY

By EDWIN B. CONNOLLY
Vice-President.

8 COUNTY OF NEW CASTLE
State of Delaware ss:

Edwin B. Connolly, being duly sworn, deposes and says that as Vice-President of Canadian-Pharmaceutical Company, the above-named Plaintiff, he has read the foregoing Complaint by him subscribed; that the same is true of his own knowledge and belief, except as to matters therein stated to be alleged upon information and belief, and as to those matters he believes it to be true; that Plaintiff is a corporation and affiant makes this affidavit in verification for it on its behalf and he is duly authorized to do so.

EDWIN B. CONNOLLY

Subscribed and sworn to before me this 13th day of November, 1939.

J H CASSIDY

(SEAL)

Notary Public.

Copy served by registered mail on Attorney General of the United States.

9 *B. Answer to the Complaint.*

To the Honorable the Justices of the District Court of the United States for the District of Columbia.

1. Defendant admits the allegations of plaintiff's organization and principal place of business.

2. He admits the allegations of defendant's official position, citizenship and official residence in the District of Columbia.

3. He admits the allegation of jurisdiction under Section 4915 R. S. (U.S.C., title 35, sec. 63.)

4. He admits that Hendry C. Connell, M.D., claiming to be the first, sole and original inventor of an alleged "New Pain-Alleviating Material", filed an application for patent thereon in the Patent Office on April 20, 1937. He admits that said application was in accordance with the requirements of law.

10 5. He admits that said application was in due form and particularly pointed out and distinctly

claimed the alleged invention of Hendry C. Connell, M. D., and that said application was given Serial No. 137,931.

6. He admits that said Hendry C. Connell, M.D., duly prosecuted said application and clearly pointed out therein his alleged invention. He admits that plaintiff should furnish a duly certified copy of said application and proceedings thereon at the trial.

7. He admits that said application of Hendry C. Connell, M.D., is directed to a type of subject-matter which is embraced within the statutory classes of inventions on which patents may be granted.

8. He admits that plaintiff believes that the applicant Hendry C. Connell, M.D., was entitled to a patent containing claims numbered 2, 3, 4, and 6 to 12, inclusive, of said application, which claims are as set out in paragraph 8.

9. He admits that the examiner made the statement quoted in paragraph 9.

10. He admits that the examiner made the statement quoted in paragraph 10. He denies that the examiner conceded that the alleged invention defined by claims 2, 3, 4, and 6 to 12, inclusive, is sufficiently important to justify the issuance of a patent containing any of said claims.

11. He admits that the examiner rejected said claims on the ground that the alleged invention defined thereby is not of sufficient importance to justify the issuance of a patent therefor under the provisions of Section 4893 of the Revised Statutes. He denies that said rejection was erroneous.

12. He admits that the Board of Appeals in its decision rendered on June 5, 1939, made the statement quoted in paragraph 12. He denies that the Board conceded that the alleged invention had sufficient utility to warrant the grant of a patent containing any of the claims set out in paragraph 8.

13. He admits that the Board of Appeals, in its decision rendered on June 5, 1939, made the statement quoted in paragraph 13.

14. He admits that the Board of Appeals, in its decision rendered June 5, 1939, affirmed the action of the examiner in rejecting the claims numbered 2, 3, 4, and 6 to 12, inclusive. He denies that the decision of the Board of Appeals was erroneous.

15. He admits that no appeal from the decision of the Board of Appeals was taken to the United States Court of Customs and Patent Appeals.

16. He admits the allegation of assignment as set forth in paragraph 16.

17. He admits that he has refused and still refuses to grant letters patent on said application containing any of the claims 2, 3, 4 and 6 to 12, inclusive. He denies that plaintiff is lawfully entitled thereto as it is deemed that the alleged invention set forth in said claims is not sufficiently useful or important to justify the issuance of a patent, as is evidenced by the following publications, and for the reasons given in the statement of the examiner in answer to the appeal and the decision of the Board of Appeals, copies of which will be furnished at the trial:

American Journal of Cancer, Jan. 1936, pp. 214 and 215, article by Gye and article by R. F. Wright,

Proc. Soc. Exp. Biol. and Med., June, 1936, pp. 581 to 584, Article by Rusch and Preston,

Journal A.M.A., May 9, 1936, pp. 1654 to 1657, article by Pommerenke,

Am. J. Cancer, Oct. 1938, p. 295, abstract of article by Goldfeder.

Profert of copies of these articles is hereby made.

W. W. COCHRAN

*Attorney for Commissioner of
Patents, Defendant.*

December 9, 1939.

I hereby certify that a copy of this Answer was mailed to the attorney for plaintiff on December 9, 1939.

W. W. COCHRAN

Attorney for Defendant.

II. APPELLANT'S PROOFS.

- 13 *A. Interrogatories Under Rule 31 Propounded to James Cameron Connell, M.D., and His Answers Thereto.*

Direct Interrogatories.

Interrogatories to be propounded to James Cameron Connell, M.D., witness for the plaintiff in the above entitled action, residing at 265 King Street, Kingston, Ontario, Canada, by David J. Rankin, Esq., c/o Day & Rankin, 69 Clarence Street, Kingston, Ontario, Canada, a notary public for the Province of Ontario:

Question 1. Please state your full name, age, residence and education.

651 A. James Cameron Connell. 77. 350 King St. West, Kingston, Ontario, Canada. M.A., Queen's University, 1885. M.D., C.M., Queen's University, 1888. M.D., Toronto University, 1888.

Q. 2. Describe briefly your experience since graduating from medical school.

A. In active practice since 1888 in the City of Kingston. Surgeon to the Kingston General Hospital, 1889 to 1929. Professor, Queen's University, 1889 to 1929. Dean Medical Faculty, Queen's University, 1902 to 1929. Acting Principal, Queen's University, 1929. Member, Education Committee, College of Physicians, Ontario, 1917-1929.

652 Member, Education Committee, Medical Council of Canada, 1912 to 1929.

Q. 3. State the medical and other learned societies in which you have held membership.

A. Local—Kingston Medical and Surgical Society. Provincial—Ontario Medical Association College of Physicians and Surgeons of Ontario. Dominion of Canada—Canadian Medical Association Medical Council of Canada. United States—American College of Surgeons American Trilogical Society. Great Britain—British Medical Association.

Q. 4. State the offices which you have held in these societies.

A. Local—One of the Founders of the Kingston Medical and Surgical Society in 1892. President for several years. Provincial—Member of the Ontario Medical Association since 1888. Honorary Member since 1929. Member of the College of Physicians and Surgeons since 1888. Member of the Council of the College 1916 to 1929. Member of the Education Committee of the Council, 1916 to 1929 and Chairman for some years. Dominion—Member of the Canadian Medical Association since 1888. One of the Founders of the Medical Council in 1912. President of the Medical Council of Canada, 1915-16. Member of the Council from the date of its formation in 1912 to 1929. Member of the Education Committee throughout that period and Chairman of the Committee for some years.

Q. 5. Have you been the recipient of any honors in the medical or educational field?

A. Yes, especially in the field of medical education.

14 Q. 6. State what these honors were and from whom they were received.

653 A. President of the Kingston Medical and Surgical Society for several years. Honorary Member of the Ontario Medical Association in 1928 for services to medical education. Member of the education committee of the College of Physicians and Surgeons of Ontario from 1918 to 1929 and Chairman of the committee for several years. President of the Medical Council of Canada 1915-16. Member of the education committee of the Medical Council of Canada from 1912 to 1929. Chairman of the education committee for several years. Honorary Degree of LL.D. from Queen's University in 1929. Dean of the Medical Faculty of Queen's University from 1902 to 1928. Acting Principal, Queen's University, 1929.

Q. 7. State briefly why you are unable to leave the environs of Kingston, Ontario.

A. Unable to travel owing to results of an accident,—fracture of hip, and other infirmities due to age (77).

Q. 8. How long have you been interested in the study and treatment of cancer?

A. Fifty years or more,—to be exact since 1884.

Q. 9. What are the recognized methods of cancer treatment?

A. In my early days of practice, surgery and caustics were the only methods of treatment employed. These were limited in application by the situation of the cancer and by the restricted field of surgery at that period of its development. Between 1895 and 1900 X-rays were found to be of use and few years later radium was discovered and employed in cancer cases.

Since that time, it is commonly stated that surgery, and radiation with X-rays and radium are the recognized and generally accepted methods of treatment of cancer.

Q. 10. How long have X-ray and radium been recognized methods of treating cancer?

654 A. X-rays were discovered in the fall of 1895 by Prof. W. K. Rontgen. The striking attribute of these rays was their power of penetrating objects which were opaque to ordinary light. Potential value in the realm of medicine was at once recognized. In 1897 it was found that the X-rays had a specially selective action on cancer cells and from that date experimental use of X-rays in the treatment of cancer gradually developed. Radium was discovered by the Curies in 1898 and soon afterwards it entered into competition with X-rays as a method of treatment of cancer.

Q. 11. How long did it take the medical profession to accept X-ray and radium as cancer treating adjuncts after they had first been used for this purpose?

A. Fifteen to twenty years.

Q. 12. What was the early attitude of the medical profession with respect to the use of X-ray and radium in the treatment of cancer?

A. At first skeptical and critical, then very slow to accept reports published as correct. Ridicule and abuse heaped upon the early advocates, retarded its use and deprived many victims of cancer of the benefits to which they were entitled. Confirmation of this can be obtained by reference

to the medical press of the period between 1895 and 1920. The following quotation was written more than ten years after it became known that radiation was of use to control malignant disease.

From the Memoirs of Sir Almeric Fitzroy, Clerk of the Privy Council.

“I have been obtaining information for the Prime Minister on the subject of a Royal Commission on cancer. Lords Lister and Rayleigh were the obvious people to appeal to, though in the present state of medical opinion nothing but a dubious judgment could be expected. Lord Lister wrote very courteously but expressed nothing more than the opinion of the medical authorities, which I knew
655 would be unfavorable to investigation by any independent body. Lord Rayleigh disclaimed any qualification to speak on his own responsibility, but undertook to ascertain whether the Council of the Royal Society would advise on the point. The medical profession will hear of nothing but the surgical treatment of cancer, partly because of its traditional repugnance to the introduction of new methods and possibly owing to the enormous profits that accrue from operations for cancer.

“Jenner, Simpson, and to a lesser extent, Pasteur and Lister, have all in turn had to encounter the opposition of the Mandarins of the profession.”

Q. 13. Upon what do you base your answer to the last question?

A. First, upon personal knowledge and experience. I lived through this period and was in daily contact with many members of the profession as well as being a reader of the medical press. Second, upon records and reports in the medical press of that period. For example, there is an editorial in the London Lancet of Nov. 18, 1911, on Cancer Research which deals with operative treatment only. X-rays and radium are not even mentioned. In 1905, Journal of Medical Research, Nov. 28th, there is an article by Vose and Horven containing a report on 120 cases of cancer treated with X-rays with the following conclusion,—“Great claims

were made for the use of Rontgen rays but at present much of the confidence at first felt has gone. Failure to effect any good in many cases of epithelial cancer and all cases of deep-lying cancer must discourage its use in such cases. Its value is limited to superficial cases which are more easily dealt with by surgery."

Q. 14. State the pertinent excerpts from this report.

656 A. A copy of the report of the London Cancer Commission is not available and for that reason I am unable to give excerpts from that particular source. However, I am able to quote from the London Lancet issued during 1910 which have the same value. In the London Lancet of July 28, 1910, appears a report of the Imperial Cancer Research Fund. It was stated by Dr. Balfour, Chairman of the meeting, that "it would be a cruel kindness to suggest that we are even within sight of anything that can be called a new remedy for cancer." Removal of cancer by operation is the only treatment mentioned. Lancet, 1910, Vol. 1, page 267-8. At the annual meeting of the British Medical Association Dr. Gilbert Barling gave the address in surgery and in the course of it discussed the nature and remedies for cancer. He acknowledged the value of X-rays in some forms of malignant disease but stated he had never known a growth certainly malignant to disappear under X-rays and he did not assent to the claims made for the rays. In 1910 the International Conference on Cancer met in Paris. See Lancet, 1910, Vol. 1, page 1108. Professor Delbert stated cancer was curable, the only proper treatment being a surgical operation for its removal. The use of X-rays was not discussed by the conference.

Q. 15. Are you acquainted with United States patent application Serial No. 137,931, entitled "New Pain Alleviating Material," filed in the United States Patent Office by Hendry C. Connell, on April 20, 1937?

A. Yes.

15 Q. 16. How long have you been acquainted with the work upon which this patent application was based?

A. Since its inception in 1934, as well as with the preliminary work which led up to it. This began in 1930.

Q. 17. Approximately how much money has been spent in the development of the invention described in the aforesaid patent application?

657 A. From August, 1935, to May, 1940, the amount spent was \$217,000.00. In addition to this amount valuable services were rendered by many people without remuneration.

Q. 18. How many case histories of patients treated with this product have you personally examined?

A. Between eighteen hundred and two thousand. Approximately all the case histories available at the Foundation.

Q. 19. How long has this product been used in the treatment of cancer patients?

A. The first injection of this product in a case of cancer in a human being was made on May 12, 1935. I saw this case and the reactions which followed the use of this product.

Q. 20. How many doctors have administered this product in the treatment of their cancer patients?

A. Impossible to give the exact number. It is however, in excess of one thousand.

Q. 21. How many of these doctors were personally unknown to the originator of this product and his associates in the Hendry Connell Research Foundation, Limited?

A. 95% at least.

Q. 22. Is it true then that the great majority of physicians who have used this treatment and whose case histories have been examined by you are personally unknown to you and your associates and have no interest in this product other than to the extent that it may benefit their patients?

A. Yes.

Q. 23. What is the concensus of opinion of these physicians as to the pain alleviating properties of this product, based upon the case histories which you have received from them and examined?

A. The almost unanimous opinion of these physicians is that the use of this product alleviated the pain in cancer. It also produced other beneficial effects and no harmful reactions have ever been observed or reported.

Q. 24. Approximately how many injections of this product have been given and over what period of time?

A. Cannot approximate the number. Tens of thousands have been given over a period of five years.

16 Q. 25. Would you have been advised of any injurious results if they had been obtained from the use of this product?

A. Yes, certainly.

Q. 26. Were you ever so advised?

A. No.

Q. 27. Has this product ever caused harm to any of the patients into whom it has been injected, so far as you know?

A. No. None have been observed or reported.

Q. 28. From your own personal knowledge has this product been of value in the alleviation of pain due to cancer?

658 A. Yes, unquestionably so.

Q. 29. Have any of the cancer patients or case histories which you have examined evidenced that this product is of value in the alleviation of pain due to cancer?

A. Yes, ample evidence which is accumulating every day.

Q. 30. Approximately what percentage of cancer patients, wherein pain is a symptom, have experienced alleviation of pain by the use of this product?

A. Above 90%.

Q. 31. Upon what do you base your answer to the last question?

A. My answer is based upon a personal study of the case histories of 382 cases of cancer in relation to pain. Of these 24% had no pain or pain was so slight in character that medication for its relief was not required. 289 cases required drugs in some form for the relief of pain. These 289 cases were treated with this product and in 279 or 96%, pain was partially or completely relieved. This study has

been published and the percentages have not been questioned.

Q. 32. What has heretofore been the customary method of relieving pain due to cancer?

A. The use of morphia or its derivatives.

Q. 33. Is this method completely successful?

A. No, not in any case.

Q. 34. What are its disadvantages?

A. All the well-known disadvantages and objections connected with the use of morphia, especially in chronic cases of pain. Gradually increasing doses are necessary to give relief, the relief afforded is transient, the systemic disturbances which result and the final failure to produce relief with enormous doses.

Q. 35. Are these disadvantages recognized and admitted by the medical profession?

A. Yes and as well known to the laity as to the medical profession.

17 Q. 36. Has the product described in the patent application previously referred to evidenced properties superior to the pain alleviants about which you have just testified?

A. Yes, decidedly so.

Q. 37. In what respects is this product superior to the pain alleviants previously used?

659 A. The product in question is not habit forming; in many cases the relief is immediate and complete, there are no systemic disturbances and natural sleep is secured. There are also other beneficial results from the use of this product. Appetite improves, weight is increased and there is a general sense of well-being created.

Q. 38. What is the basis for your answer to the last question?

A. First my personal observations and second, the observations and experience of hundreds of physicians and patients.

Q. 39. Is this product capable of use in conjunction with surgery, X-ray and radium treatment?

A. Yes, There is no contraindication to the use of this product.

Q. 40. Is this product of value after these recognized forms of treatment are no longer applicable?

A. Yes.

Q. 41. Upon what do you base your answer to the last question?

A. Upon personal knowledge and the information contained in the case histories of a large number of such cases of cancer.

Q. 42. Is the pain alleviating property of a product customarily determined by treating patients with it?

A. Yes, Such tests can only be made by the use on patients. Animal experimentation can never elucidate pain relief. The suffering patient is the last court of appeal and the physician accepts his verdict as to the results which follow the use of any remedy.

Q. 43. Have the tests applied to the product described in the aforesaid application been as thorough as the tests customarily applied to determine pain alleviation?

A. Yes. These tests have been much more thorough than is customary in evaluating pain alleviation.

Q. 44. Is there a great need for a pain alleviant in the treatment of cancer?

A. Yes.

Q. 45. Why?

A. First, because of the severity, intensity and prolonged nature of the pain in many cancer cases, and, second, because of the unsatisfactory character of the presently available remedies.

Q. 46. Is the product of the aforesaid patent application an important contribution to the problem of pain alleviation in the treatment of cancer?

660 A. Yes, Important in itself and also because it opens up a new field of investigation in the cancer problem.

18 Q. 47. In your opinion is the product described in the aforesaid patent application harmless and of appreciable value in the alleviation of pain due to cancer?

A. It is harmless. No ill effects have been observed or reported from its use. Its value has been amply proved over a five year period of use.

Q. 48. Upon what do you base your answer to the last question?

A. Upon personal experience and that of hundreds of physicians and patients over the past five years.

Q. 49. In your opinion, is this product superior to any of the pain alleviants previously used for the treatment of cancer?

A. Yes. I give it preference in any case coming under my care or observation.

Q. 50. Upon what do you base your answer to the last question?

A. Upon experience and observation as recorded.

Q. 51. Has the product described in the aforesaid patent application been investigated by any authoritative group not connected with the inventor thereof or the Hendry Connell Research Foundation, Limited?

A. Yes.

Q. 52. What was the name of this group and to whom did it present its findings?

A. The Commission for the Investigation of Cancer Remedies appointed by the Legislature of the Province of Ontario. Its findings have been presented to the Minister of Health of the Province of Ontario in the form of two reports which were submitted by him to the Legislature.

Q. 53. Did this group find that this product was harmless?

A. Yes.

Q. 54. Did this group find that this product was of value in the alleviation of pain due to cancer?

A. Yes.

Q. 55. Did this group render an official report based upon its investigation?

A. Yes.

Q. 56. When and to whom was this report rendered?

A. Two interim reports have been made to the Minister of Health of the Province of Ontario. First Report, January, 1939. Second Report, January, 1940.

19 Q. 57. Kindly quote therefrom the excerpts which led you to state that this product was harmless and was of value in the alleviation of pain due to cancer?

661 A. From the first report,—“Conclusion No. 2. From the evidence Ensol (the product in question) was shown to be harmless when prepared, distributed and administered under rigid control.”

“In the great majority of cases treated there appears to be relief of pain.”

From the second report,—“It seems clear from the evidence of case histories, physicians’ reports and the examination of patients that Ensol (the product in question) used according to directions, is harmless and that it produces no undesirable immediate or remote effects.”

“Improvement is manifested by lessening of pain and tension.”

Q. 58. Has this report been accepted by the Ontario Government?

A. Yes and presented to the Legislature.

Q. 59. As a result of this report, did the Ontario Government evince any interest in this invention?

A. Yes.

Q. 60. How was this interest demonstrated?

A. The first report of the Cancer Commission recommended that the research should be continued by the Foundation and that some arrangement be made to have the work of the Foundation assisted by experts independently of the Foundation staff. This was done by the Minister of Health appointing a clinical consultant and an experienced laboratory expert and by setting up a laboratory near that of the Foundation in Kingston to work independently but in co-operation with the Foundation. This laboratory has its own staff. A preliminary report was made to the Minister after the first six months of work and that was before the Cancer Commission when the second report of that body

was made. After the second interim report of the Commission was considered by the Government and submitted to the Legislature it was decided by the Government that the Foundation should continue to work separately and that financial assistance should be given to enable it to do so.

That was done. Since the first of January, 1940, 662 the expenses of the research and of the manufacture and distribution of the product for clinical use have been fully met by the Ontario Government. That is in addition to the support of its own special laboratory in Kingston.

Q. 61. Has the Ontario Government ever borne the research expenses of any other independent body working on a new product for use in the treatment of cancer?

A. No.

Q. 62. Has this Government investigated other cancer treatments?

A. Yes, through the Cancer Commission which was appointed for that purpose.

Q. 63. Has it ever offered to bear any of the research expenses on these other cancer treatments which it has investigated?

A. No.

Q. 64. Are you generally acquainted with the Biochemical Research Foundation located in Philadelphia, Penna.?

A. Yes.

Q. 65. Are you acquainted with the catastrophe which occurred in Florida sometime ago due to the administration of a product produced by this Biochemical Research Foundation?

A. Yes.

Q. 66. Was that product the same as the product described in the aforesaid patent application?

A. No. That product was quite dissimilar to the product described in the aforesaid patent application?

20 Q. 67. Is there any relationship between the Hendry Connell Research Foundation, Limited and the Biochemical Research Foundation?

A. No.

Q. 68. Is it unusual to use diseased tissue or toxic organisms in the preparation of a harmless and beneficial therapeutic?

A. No. Notably for example, the use of the spinal cord of a rabid animal to produce a remedy for rabies (Hydrophobia) and also the use of tuberculosis organisms to produce a remedy for tuberculosis.

Q. 69. Is the cancer tissue completely destroyed in the preparation of the product described in the aforesaid patent application?

A. Yes. The cancer tissue is completely digested and the solutions used for injection are sterile.

Q. 70. Are the micro-organisms used in the preparation of this product completely destroyed before the product is injected into patients suffering from cancer?

A. When the digestion of the cancer tissue is completed the micro-organisms are removed from the solution by filtration. As already stated, the product is sterile and remains so indefinitely.

Q. 71. Is there then anything repugnant to recognized and sound biochemical practices in the preparation of this product and its use upon human beings?

663 A. No. Recognized and sound biochemical practices are followed in the preparation of this product and its use upon human beings.

Q. 72. What is the basis for your last answer?

A. My knowledge of well-recognized and sound biochemical practices in the preparation and use of various serums, toxins and similar products. I have watched the introduction, development and use of these during my professional life.

Q. 73. Have you personally examined all the case histories described in the three bulletins published by the Hendry Connell Research Foundation, Limited on this product?

A. Yes.

Q. 74. How many case histories are described in each of three bulletins?

- A. Bulletin No. 1. 116 cases
 2. 159
 3. 139
-

414 cases

These comprise a fair cross section of more than a thousand case histories.

Q. 75. Approximately how many injections of this product were given to the patients described in each of these bulletins and over what period of time?

A. An accurate estimate of the number of injections of this product would be impossible since it is given by hundreds of independent physicians throughout the world who do not report the individual injections given. However, a conservative estimate is that tens of thousands of these injections have been given over a period of five years.

21 Q. 76. Were any harmful effects observed or reported as a result of the use of this product on any of the patients, so far as you know?

A. None whatsoever.

Q. 77. How many of the case histories described in the three publications of the Hendry Connell Research Foundation, Limited mentioned pain as a symptom?

A. That record was not kept. However, 382 cases of cancer treated at the Foundation Clinic were studied in relation to the symptom of pain. Of these 93 or 24% had no pain or it was of so slight a character that treatment for its alleviation was not necessary. 289 cases required drugs in some form for relief of pain. All these received treatment with the aforesaid product. In 279 or 96% pain was partially or completely relieved.

Q. 78. In how many of these cases was pain due to cancer alleviated by the use of this product?

664 A. In the series of cases studied in relation to pain 96% of those patients which experienced pain had partial or complete alleviation due to the use of this product.

Q. 79. In how many of these cases were there any harmful reactions due to the use of this product?

A. In none whatsoever.

Q. 80. How many different physicians treated the cases which experienced pain as a symptom of the disease, referred to in your answer to Interrogatory No. 77?

A. More than two hundred different physicians treated the cases referred to in Interrogatory No. 77.

Q. 81. Where were these physicians located?

A. These physicians were located in every Province of Canada, almost every State in the United States, in Australia, in Cuba and some other foreign countries.

Q. 82. Did you or any member of the Hendry Connell Research Foundation, Limited have any contact with the great majority of these physicians other than that which came from forwarding this product to them with instructions for its use and receiving from them reports on the success of their personal treatments?

A. No, the great majority of these physicians were personally unknown to me and, so far as I am aware, to any member of the staff of the Hendry-Connell Research Foundation, Limited. Our sole contact with them arose when they request a supply of the pain alleviating product, about which I have testified, with instructions for its use. A supply of this product and the necessary instructions were forwarded to them free of charge and the request was made that they report on the results of their treatment. These reports which I have referred to in the preceding interrogatories were prepared by unbiased and capable physicians who had no interest in this product except to the extent that it helped their patients.

Q. 83. Who is Dr. Neville Davis?

A. Neville Davis, M.B., Ch.M. (Sydney, Australia). Dr. Davis is a surgeon living in Sydney, Australia, Member of the staff of one of the leading hospitals there; once a member of the staff of the Mayo Hospital, Rochester, Minn. and in practice in Sydney for more than twenty years.

Q. 84. What is the conclusion which he reached in his article entitled "Treatment of Cancer with Ensol", with respect to the harmlessness and pain alleviating properties of this product?

A. Dr. Davis writes,—“Ensol injections do not cause patients any serious discomfort. On the contrary, even in extreme cases with ultimate death of the patient, it has been shown to give relief of pain, diminish the quantity of opiates used, improve appetite, increase weight, generally relieving distressing symptoms,”

Cross Interrogatories Under Rule 31 Propounded to James Cameron Connell M.D. and His Answers Thereto.

X-Q. 85. Are you related to Hendry C. Connell, the applicant herein?

A. Yes.

X-Q. 86. If your answer to X-Q. 85 is in the affirmative, what is that relationship?

A. Father.

X-Q. 87. Is it not a fact that in some cases treated by the product of the application in suit the patients complained of increased severity of pain?

A. Certain tumor reactions follow the use of injections of the product of the application in suit. These sensations are experienced within the tumor mass or in the region of the lesion and are described by patients as a prickling, burning, tingling or a fulness, drawing or distress, often as a pain where none existed before, or increased pain, if it were already present. These sensations come on usually several hours after the injections but they may be earlier or later and they may continue for variable periods.

The only known reaction analogous to this is the so-called Jarisch-Herzheimer reaction in syphilis observed after the injection of arsphenamide.

Transient pain of this character is the only form of pain which has been observed or reported following the use of this product. Except this reaction pain I have no knowl-

edge of increased severity of pain taking place after the use of this product.

These reactions, including pain, do not occur if the dose of the product is slightly reduced. They are, however, regarded as definite evidence of the specific action of this product on the tumor mass. With a reduced dose the pain subsides and being maintained at that point, the pain is brought under control.

This reply is in accord with a statement submitted to the Ontario Commission for the Investigation of Cancer Remedies. Copy of this is attached.

X-Q. 88. Are you familiar with the work of Rusch and Preston, Pommerenke, Gye and Goldfelder in connection with the product of the application in suit?
24
666 A. Yes.

X-Q. 89. If so, state whether you agree or disagree with their conclusions in respect to the use of this product in the treatment of cancer.

A. I disagree entirely with their conclusions in respect to the use of this product in the treatment of cancer?

Re-direct Interrogatories Under Rule 31 Propounded to James Cameron Connell M.D. and His Answers Thereto.

Re-D. Q. 90. State in detail your reasons for your answer to X-Q. 89.

A. The work of Rusch and Preston, Pommerenke, Gye and Goldfeder in connection with the product of the application in suit is of no value for the following reasons,—

1. No part of their work dealt with pain relief which is the basis of this application.

2. Their experimental work was conducted upon mice. Pain relief cannot be proven by animal experimentation. No clinical work was undertaken by any of these investigators although opportunity was afforded them to do so.

3. Experiments conducted by these men were for the purpose of determining whether tumors in cancerous mice were retarded or dissolved by injections of this product.

4. Their work was carried on independently of the inventor although they were invited to visit his laboratory and learn directly what was being done therein.

5. There is no evidence that the product employed by these men was similar to that of the product in question.

6. Experiments reported by these men were completed within a few weeks. It is obvious that their work was superficial and inadequate, performed without full knowledge of the factors involved, undertaken without the co-operation of the inventor although that was tendered and available and without knowing the details of the process of manufacture and method of administration.

7. In the case of Gye, some months after he published his reports in 1935, his assistant wrote to ask how the solution was produced. In the course of correspondence
667 Gye refused to revise his work with the assistance and co-operation of the inventor.

8. These investigators conducted their experiments upon the supposition that the active principle in the solutions is an enzyme, whereas it is known to be antigenic in character. This alone renders the work of no value.

9. There is no reference in any of these publications to pain alleviation.

10. From the general scientific point of view, negative results published as these were are of no value whatever.

11. Neither in relation to the alleviation of pain nor in the broader question of the treatment of cancer are these published reports of the least value.

12. None of these individuals had before them all the facts applying to the teachings contained in the patent application in suit. These facts had not been made public or

disclosed to any of them at the time the articles were published. They failed to take advantage of an invitation to visit the laboratory of the inventor to see and learn what was being done.

Re-D. Q. 91. Did the publications of any of the individuals referred to in X-Q. 88 pertain either directly or indirectly to a determination of pain alleviation?

A. No.

Re-D. Q. 92. State your reasons for your answer to the preceding interrogatory.

A. No reference can be found in any of the publications in question to pain relief or to the clinical use of the product. Pain relief can only be determined by clinical use of the product in question or of any other substance by clinical use upon human patients who are suffering pain. No clinical use was reported by any of the investigators mentioned in cross interrogatory No. 88. It is absolutely impossible to learn anything about pain control or relief by tests upon animals.

JAMES CAMERON CONNELL

Certificate.

668 I hereby certify that the hereintofore answers to Interrogatories, to Cross-Interrogatories and to Redirect Interrogatories were given to me by James Cameron Connell, M.D., at his home, King Street West, Kingston, Ontario, where he is confined by reason of infirmity, after he had been first duly sworn to tell the truth, the whole truth and nothing but the truth, and that the answers of the said James Cameron Connell, M.D., were taken down and transcribed by Helen Jean Atkinson, a stenographer, she having been first sworn to faithfully take down and transcribe the said answers.

Witness my hand and seal at the City of Kingston this 23rd day of July, 1940.

D. J. RANKIN

*A Notary Public in and for the
Province of Ontario.*

I hereby certify that the hereintofore answers to Interrogatories, to Cross-Interrogatories and to Redirect Interrogatories were read over and signed by the said James Cameron Connell, M.D., this 23rd day of July, 1940.

D. J. RANKIN

*A Notary Public in and for the
Province of Ontario.*

(Notarial Seal)

* * * * *

B. Testimony Given Before District Court.

44 **Dr. Hendry C. Connell** was called as a witness for and in behalf of the plaintiff herein, and having been duly sworn by the Clerk of the Court, assumed the witness stand and, upon examination, testified as follows:

Direct examination

By Mr. Connolly:

Q. Will you state your full name, age, and residence, Doctor Connell? A. Calvin Hendry C. Connell, age forty-five and one-half years; residing in Kingston, Ontario, Canada, a Canadian citizen.

Q. You are a Canadian citizen? A. Yes.

45 Q. Will you describe, please, briefly, your education and experience? A. My early education was in the public schools of Kingston; my high-School education in the Kingston Collegiate Institute; I entered Arts at the Queens University at Kingston and graduated in Arts with a B.A. in 1915.

I then entered medicine, during the war years, and graduated in medicine in the winter of 1917 and '18; I then went directly into the Army Medical Corps and was posted to a hospital which went to Siberia.

I was there approximately a year on service.

At the end of the war I returned to Canada and entered the practice of eye ear nose and throat diseases with my

father, who was a well known eye, ear, nose, and throat specialist at that time in Kingston. After practicing with him for approximately about a year, till 1921 or '22, I went to the old country to take post-graduate studies. I did post-graduate work in Edinborough and in Glasgow, and then at Moorefield Eye Hospital in London, and then went to Vienna, where I studied, particularly, mastoid work, and to Berne, Switzerland, and studied and I went to Paris to see the clinics and hospitals, and I worked down there, and I then returned to Canada and practiced with my father in the practice of eye, ear, nose, and throat, until the summer of 1935, when I found myself forced to go into this research.

The background of that is due to the course of my eye work, I had a yen to discover why certain cataracts—

46 Q. (interposing) Doctor, if you don't mind, we will take that up a little later.

Would you mind telling us what your present occupation is or profession? A. Very well. I am a physician and at present I am president of the Hendry-Connell Research Foundation in Kingston.

Q. What is the Hendry-Connell Research Foundation?

A. The Hendry-Connell Research Foundation is an incorporated company, under charter, Dominion charter; it is entirely a charitable organization, incorporated for the purpose of conducting research work and the problems associated with Ensol and cancer.

Q. What is the personnel of the Hendry-Connell Research Foundation? A. At present we have three directors and a staff of ten people: myself as president and director of the actual research, a secretary, a colloidal chemist and his two assistants, a serologist and two assistants with him, and then, in the department that manufactures this material for clinical distribution, free of charge, we have two expert men beside the boy-washers, et cetera, making ten in all.

Q. Are you the Hendry C. Connell referred to in the patent application in issue? A. I am.

Q. That is now in evidence as Plaintiff's Exhibit
47 No. 1? A. I am.

Q. Are you familiar with that patent application and the proceedings had thereunder? A. Yes.

Q. Would you mind describing briefly the origin and development of the invention described therein? A. I started out to do some work while in practice in order to discover why cataract lens material did not absorb as well in certain material, particularly in older people than younger.

I worked at that time, in spare hours and at night, and, following my practice hours in the office, and I was successful in obtaining a grant from the National Research Council in Ottawa. My idea was at that time possibly if we could find some enzyme that could be injected into the eye we would aid or hasten the absorption of the lens material which was opaque and which would obstruct vision.

Lacking the source of such an enzyme and knowing all body enzymes were successfully recovered from the leukocytes, we used animals to get sterile exudate from the serum and we washed the cells and were able to recover an enzyme solution which, when added to this cataract lens material in vitro tests, showed a very marked increase in the digestive procedure.

Then we produced traumatic cataracts on rabbits with the idea of attempting to have them absorbed by the
48 addition of these enzyme solutions.

We were successful in the attack on the lens protein with the body enzymes, but although the experiment was successful, the whole eye was attacked; there was no control over that and, therefore, it was necessary to attempt to produce a specific type of enzyme. In our search for this we went to the proteolytic organisms with the expectation that possibly we might be able to grow a proteolytic micro-organism on lens protein and thereby recover a specific enzyme.

We did this, and during the course of this work—it was successful in vitro—and during the course of this work it

occurred to me that possibly we could use the same process on other protein, foreign protein, of the human body. Naturally, cancer was the first and most serious disease, and there was so little known about it that I thought possibly something might happen there.

We therefore procured some cancer tissue and grew those organisms on it and found we were able to recover a specific enzyme and, when applied in the test tube, the cancer tissue did disintegrate very rapidly.

At that time, in my practice, I had a Chinaman who had been giving me a very considerable lot of bother from the fact that he had had a carcinoma or cancer of the organ and very marked protrusion of the eyeball with very marked pain, and he had been referred by me to the radio-
49 logists and surgeons, and nothing could be done surgically and radium seemed to have no effect, and therefore he was left without hope.

He continued coming in and I was extremely busy.

One day I said to him, "Well, possibly something may be done for you." So I explained to him what we were doing, told him about our research work, and said that if he would like to take a chance on using some of the filtrate, we might see what would happen.

We made up a sterile batch of the filtrate and, before giving it to the Chinaman, I took a dose myself and, after twenty-four to forty-eight hours, when there was no danger of reaction occurring, nothing happened, I was perfectly normal, I decided that it would do the Chinaman no harm at least—at least I did not think it would—and I tried it, not with the expectation of getting any really startling result, but within a week the pain had very decidedly lessened, which we knew definitely because of the lack of necessity to keep so many sedatives going; the protrusion of the eyeball had lessened very considerably.

There was a certain loss of vision due to pressure of the tumor mass on one of the optic nerves leading to the eye, but that pressure having been released some vision came

back, and this occurred within the course of perhaps three to four weeks.

Such things I had never seen happen before in cancer patients and naturally my interest was extremely wrought up.

50 I then consulted with some of my colleagues and we consulted one of these gentlemen who had another case, a lady with carcinoma of the pelvis and ovary who had had several operations; she had been subjected to surgery, to all the known methods of relief; they had all been given her, and she now had become bedridden and was suffering very considerable pain; in fact, she was getting four grains of morphia a day.

I happened to know the family very well and one of the family was a patient who came into my office at times and had been asking me about the research I had been doing, and asked if it would be possible to try anything like this on his wife. I said it would be, but I did not know whether any results could be expected and what might happen. However, he stated that nothing further could be done for her and it seemed to be too bad to keep her on morphia and let her be left to die if anything might come of this, and he was quite willing to have it done.

I spoke to the physician and he immediately acquiesced in the attempt to treat the woman, and so we gave her some of the filtrate, not expecting, again, very much in the way of results; but this patient, as I say, was bedridden and suffering terrific pain and required a great deal of sedatives, but within two or three weeks she was off the sedatives entirely, got out of bed and felt very comfortable.

There was some tension in the abdomen and one could
51 feel a lump to begin with, and that had now receded to some extent.

That was in the spring, or in April, of 1935.

Later in the spring and early summer this lady was able to get up and do her own housework, be out in the garden; she used to do some gardening, and she swam and enjoyed

her summer very much and went through the winter and all the next spring until late in the fall, in October, I think, of the next year, when she returned to our clinic, to me, and on examination, there was a lump found again in the lower abdomen.

We naturally thought that this was a recurrence of the tumor, and, the lady having been subjected to so many operative procedures, we decided that it might be rather an ordeal to put her through any more surgical work, and, the husband thought perhaps it was best just to let it go.

Unfortunately, we did let it go and did not open up the abdomen.

She came to post-mortem. She died from an acute intestinal obstruction and, at post-mortem, the area where the tumor had been was found to be copulated, and the reason for the acute intestinal obstruction was found to be adhesions, and if we had had courage enough to open up the women she probably would be alive today.

Those are the two cases in the beginning that sort of forced me into the follow-up of this cancer work.

Q. Doctor, approximately how much money has
52 been spent in the development of this invention?

A. Approximately—well, I can give you it fairly accurately: between \$235,000 and \$245,000.

Q. In what manner was Ensol distributed? A. Ensol was distributed free to physicians who would cooperate with the Foundation in returning case histories and giving us progress notes on their cases for our files.

Q. What was the purpose of distributing this product to physicians? A. In order to get a good cross-section of the profession who would be able to give us their ideas as to what was actually happening in those cases.

Q. Approximately how many cubic centimeters of Ensol have been distributed by your Foundation to physicians, free of charge? A. All told?

Q. If you know the answer, yes. A. Over 400,000 cubic centimeters.

Q. Approximately how many physicians have received this product? A. Up in the hundreds; 600—from 600 to a thousand physicians.

Q. Have you received reports from those physicians on the progress of their patients? A. Oh, yes.

53 Q. Approximately how many of these reports have you personally examined? A. Well, I have personally examined practically all those reports.

I do not think there are very many that I could have missed.

It is my job to see that those are properly filed and gone over.

Q. How many patients, suffering from cancer, have been treated with Ensol under your direct supervision? A. Under my direct supervision I should say, including those cases treated at our own clinic in Kingston, about 800 to 1,000.

Q. Were any of those patients beyond the help of the three presently recognized forms of treatment, x-ray, radium and surgery? A. Unfortunately nearly all of them, since we did not feel justified in attempting to use this treatment on any case that could get benefit from any of the orthodox methods of treatment.

Q. In the treatment of these cases, Doctor, did you notice harmful effects in any of these patients? A. No, I have never seen a harmful effect in any one of these patients.

54 Q. In approximately what percentage of the cancer patients with whom you are acquainted was pain a symptom? A. Approximately 75 per cent of cancer patients suffer pain.

Q. In approximately what percentage of the cancer patients, suffering pain and treated with Ensol and with whom you are acquainted, was this pain reduced as a result of this Ensol treatment? A. Approximately 90 per cent, between 90 and 96 per cent, I believe.

Q. What percentage would this be of the total number of cases, Doctor, including those cases that did not have

pain as a symptom? A. Approximately—Would you repeat that question, please?

Q. What percentage of all cases would this be, including those cases that did not have pain as a symptom?

You mentioned, I believe, that approximately 75 per cent of all the cancer cases had pain as a symptom.

In those cases having pain as a symptom, as I understand you, approximately 90 per cent experienced reduction in this pain as a result of treatment with this invention, Ensol.

Now, the question was: What percentage of the total would that amount to that experienced pain reduction?

A. Approximately 65 per cent, I think.

Q. How did you determine whether there was reduction of pain in those cases, Doctor? A. A reduction in pain could be only determined by the lessening of the amount of sedatives required to ease the pain.

Q. Were any other—Excuse me. Did you finish the answer? A. There are still other clinical findings by which, of course, we are able to make the discovery: he will tell us, for instance, but the actual release of morphia and sedatives is the actual experience or index to the relief of pain.

Q. Have you ever represented Ensol as a cure for cancer? A. Absolutely no.

Q. In your judgment, based upon your experience with cancer, would you consider that a product which is capable of reducing pain due to cancer in approximately 65 per cent of the cases is a valuable contribution to the medical practitioner? A. Very decidedly.

Q. Would you mind mentioning, Doctor, what procedure was used in controlling or reducing pain in cancer patients prior to this discovery? A. The only method of control of pain was the use of sedatives, particularly morphia and its derivatives.

Morphia and its derivatives are, of course, habit-forming drugs.

Naturally one held off using morphia until it had to be used; then it was found very often a tolerance in the

56 patient was developed and gradually higher and higher doses had to be given which is, really, not a very satisfactory method of control.

Q. Do I understand, then, that morphia and other sedatives are not considered to be satisfactory in the treatment of cancer for the alleviation of pain? A. They are for the control of pain but do not treat the disease; they deaden the pain but do not reduce the cause.

Q. I hand you Bulletin No. 3 of the Hendry-Connell Research Foundation, which is Plaintiff's Exhibit No. 4, and I refer you to pages 126 and 127 of this bulletin. There is an article entitled "Pain in Malignant Disease," and it is by Doctor J. C. Connell. The second paragraph of this article is as follows:

"The other 289 cases required drugs in some form for relief of pain. All these received Ensol treatment and in 279 or 96 per cent pain was partially or completely relieved. While a much larger group should be studied to give accurate percentages, it can be said that approximately 76 per cent of cases of malignant disease require medication for the relief of pain. Further it appears that 73 per cent of all cases of cancer treated with Ensol were relieved of pain in some degree."

I ask you, Doctor, are you acquainted with the 289
57 cases referred to therein? A. Yes, I am acquainted with those cases.

This article was compiled after a careful study of cases that had passed through our clinic and had particular reference to pain-relief.

Q. Doctor, do you, as a result of your familiarity with these cases, subscribe to the conclusion referred to in this bulletin in the excerpt just quoted? A. I do.

Q. Doctor, I hand you an article which purports to be a reprint from the Journal of the American College of Proctology, for December, 1938.

This article is entitled "Rectal Carcinoma, How Best Handled," and is by Doctor Thomas F. McNamara of Ro-

chester, New York, and is one that was delivered before the American College of Proctology at the fifteenth annual meeting held in the Stevens Hotel at Chicago in September, 1938.

Will you please state whether or not you are familiar with that article and, if so, will you please tell us what you know about it (handing the document under consideration to the witness)? A. (after examining the document in question) I am familiar with this work.

Before delivering this paper, Doctor McNamara wrote to me requesting my permission to do so, and that was granted.

I did not see the article before it was published
58 and I have never met Doctor McNamara, although
I know that he is a very old practitioner and one well
thought of by his colleagues.

In this article he draws attention to the fact that he has treated rectal carcinoma with the usual orthodox methods, and he says on page 6:

"Now I would like to take the time to read to you a few results from the use of Ensol, which is what I used for my patient who is still on his feet—"

meaning, of course, the other patients that had not had Ensol were not on their feet. He continues:

"There are a number of cases cited in this book but I shall read of just two.

"Biopsy proof. Symptoms present two years before positive diagnosis made. Colostomy May, 1936. Admitted June 30, 1936. Pain in lower sacral region, discharge and bleeding from the rectum. Weight 146 pounds. Ensol was used from July, 1936, to date. There has been a marked general improvement, a twenty-two pound gain in weight maintained to the present time. There is no bleeding and the discharge has been very definitely diminished. The pain symptom has been relieved and the patient has not been receiving any type of analgesic."

In the other case he cites he says:

“The pain, sloughing, bleeding, discontinued about two months after the treatment had begun.”

59 That is all I know about the case; I have never seen the case, but yet I am quite ready to accept that as an accurate description of what did happen.

Q. From your experience with the use of this product, Doctor, would you consider that these cases are typical of those treated with Ensol? A. Yes, typical, but not 100 per cent typical. One hundred per cent in medicine—they are typical of the percentage of cases that get relief from Ensol, yes.

Mr. Connolly: I should like to offer this reprint in evidence as Plaintiff's Exhibit No. 6.

(The document in question, being a reprint from the Journal of the American College of Proctology, December, 1938, entitled “Rectal Carcinoma, How Best Handled,” by Thomas F. McNamara, Rochester, New York, was thereupon received in evidence and marked by the Clerk of the Court, “Plaintiff's Exhibit No. 6.”)

By Mr. Connolly:

Q. Doctor Connell, I now hand you what purports to be a reprint from the Journal of the American College of Proctology, for March, 1939. This reprint is entitled “Ensol As An Aid In the Treatment of Rectal Cancer,” and it is by Doctor Glenn S. Burton.

Will you please state whether or not you are acquainted with the article and, if so, please tell us what you
60 know about it (handing the document referred to to the witness). A. (after examining the document last referred to) I am acquainted with this article and know that the contents are correct and based on the observation of Doctor Burton in treating those cases.

Doctor Burton states on page 2:

“Of the 59 cases of rectal cancer treated with Ensol over a period varying from two months to three and a half years,

there were 43 cases, or approximately 75 per cent, who received benefit as estimated by pain relief and symptomatic improvement."

The remainder of the article I think I need not read.

Q. Do you consider those cases a fair cross-section of the cases of this type treated with Ensol? A. Yes, I do.

Mr. Connolly: I should like now to offer this article in evidence as Plaintiff's Exhibit No. 7.

(The document in question, being a reprint from the Journal of the American College of Proctology, March, 1939, entitled "Ensol As An Aid In the Treatment of Rectal Cancer," by Doctor Glenn S. Burton, was thereupon received in evidence and marked by the Clerk of the Court, "Plaintiff's Exhibit No. 7.")

By Mr. Connolly:

Q. I now hand you, Doctor, an article entitled "Relief of Pain in Cancer by the Use of Ensol."

61 Under the title that I have just read to you the paper bears the statement:

"Submitted to the Ontario Commission for the investigation of cancer remedies by the Hendry-Connell Research Foundation."

The date is May, 1940.

Will you please state if you are acquainted with this article and, if so, tell what you know about it (handing the document referred to to the witness)? A. (after examining the document last referred to) I am acquainted with the article and the excerpts printed therefrom are excerpts from letters on file in the case histories of the cases under treatment by the Foundation.

The article starts off to say:

"About 75 per cent of cases of malignant disease require medication for the relief of pain. Morphia and its derivatives are commonly used for the purpose.

“Clinical experience during the past five years has shown that about 90 per cent of these cases with pain can be partially or completely relieved by the use of Ensol. No explanation is advanced for this pain relief.”

The remainder of the article I need not read.

Q. How many cases are described, Doctor, in this article, if you know? A. I think 152, all told.

62 Q. How were those cases selected? A. Do you mean previous to treatment?

Q. Yes, Doctor—I mean, what was the controlling thought in selecting cases for inclusion in this bulletin? Was it an attempt to include all cases you had treated or an attempt to include a certain group of those cases? A. No. It was an attempt to show where—or to prove pain relief in the vast majority of cases that had pain.

Q. In your opinion are the cases described in this bulletin a representative cross-section of those cases treated with Ensol and suffering from pain due to cancer? A. Yes, quite.

Mr. Connolly: I should like now to offer this bulletin in evidence as Plaintiff's Exhibit No. 8.

(The article in question was thereupon received in evidence and marked by the Clerk of the Court, “Plaintiff's Exhibit No. 8.”)

By Mr. Connolly:

Q. Are you acquainted, Doctor, with the published articles cited by the Patent Office Examiner during the prosecution of your application, which articles are set forth in Plaintiff's Exhibit No. 1?

I have specific reference to the articles by Gye, Rusch and Preston, Pommerenke, and Goldfeder.

I believe those articles have been placed in evidence by the defendant as Defendant's Exhibits B, 63 C, D, and E. A. Yes, I am acquainted with them.

Q. Did any of the individuals who wrote those articles, Doctor, ever request Ensol from you? A. No, they never did.

Q. Did you ever send Ensol to any of those individuals?
A. No, not to my knowledge; I do not know of any.

Q. In a determination of the property of pain alleviation or reduction, would experiments conducted on animals have any value? A. In my opinion, I cannot see the logic of that at all.

Pain relief cannot be determined in dumb animals.

Q. Do these articles describe investigations conducted on animals? A. They do.

Q. Are you acquainted, Doctor, with the disaster which took place in Florida in March, 1938, due to the use of a non-identified product in treating certain cancer patients?
A. Yes, I am.

Q. Was that product Ensol? A. No.

Q. Was that product shipped or produced by you or anyone under your supervision or control? A. No.

Q. Will you please state what you know of the
64 disaster? A. I know that the disaster was caused by there being tetanus toxin in the material administered to those patients. The patients died from the poison of the toxin.

I also know that we had absolutely no connection with the people who made that material. We did not even know that they had been sending it out at that time and yet, erroneously, it was blamed on us and, through no fault of ours, I passed through a very serious disagreeable period for a few days until the onus of the difficulty was laid in the proper place.

We have letters from the Government of Canada, the Dominion Government, and also from Doctor Harrison of the National Institute of Health, that completely exonerate us from any blame in the matter.

Q. I hand you a letter bearing the heading "Treasury Department, United States Public Health Service, National Institute of Health, Washington, D. C.," dated "April 8, 1938," and addressed to "Doctor Hendry Connell, Hendry-Connell Research Foundation, Kingston, Ontario, Canada."

This letter is signed by W. T. Harrison, Chief, Division of Biologies Control.

Is that, Doctor, one of the letters to which you have just referred (handing the paper writing in question to the witness)? A. (after examining the document last referred to) Yes; this is one of the letters to which I refer.

65 Q. You stated, I believe, that that letter completely absolves you and your product of any responsibility due to this disaster in Florida? A. Yes.

Q. Will you kindly quote the excerpts thereof which bear on this point? A. (reading)

“Dear Doctor Connell: For your information, I have to report that the animal tests have been carried out on Ensol, lots 10,168, 10,170, 10,171, 10,175, 12,110 and 12,111. All mice injected with these lots have survived without symptoms. It can therefore definitely be concluded that all of these lots were free from tetanus toxin and could not have been responsible for the recent deaths from tetanus which occurred in Orlando Florida.”

And he says also in the letter:

“It gives me great pleasure to completely exonerate Ensol from suspicion in connection with the incident.”

Those, I think, are the two paragraphs.

Q. Does the letter contain any other information? A. The letter contains other information and suggestions made by Doctor Harrison when he was at our laboratory by which we might improve the methods of shipping and so on.

Q. Were those suggestions ever carried into effect? A.

As soon as humanly possible after Doctor Harrison
66 left we certainly did do the things he suggested, as they were really helpful.

Mr. Connolly: I now offer this in evidence as Plaintiff's Exhibit No. 9.

(The letter last referred to was thereupon received in evidence and marked by the Clerk of the Court “Plaintiff's Exhibit No. 9.”)

By Mr. Connolly:

Q. Doctor, I hand you a letter headed "Post Office" and bearing the typewritten designation "Ottawa, Ontario, April 11, 1938," and signed "H. Fortier, Chief Inspector."

Is this another one of the letters to which you referred with respect to your being absolved from all responsibility in connection with this Florida incident (handing the letter thus described to the witness)? A. (after examining the document last referred to) Yes.

Q. Will you kindly read the letter? A. Do you mind reading it? I cannot read it with these glasses.

Mr. Connolly (reading):

"Post Office, Ottawa, Ontario, April 11, 1938.

"Postmaster, Kingston, Ontario.

"Re 'Ensol' no objection to shipments being accepted for delivery in Canada and United States.

"Signed, H. Fortier, Chief Inspector."

67 I would now like to offer this in evidence as Plaintiff's Exhibit No. 10.

(The letter last referred to was thereupon received in evidence and marked by the Clerk of the Court "Plaintiff's Exhibit No. 10.")

By Mr. Connolly:

Q. Was the Hendry-Connell Foundation, Limited, ever affiliated with the Biochemical Research Foundation of the Franklin Institute? A. Yes, it was.

Q. Will you kindly state what was the reason for that affiliation? A. In the early stages of our work, after the formation of the Hendry-Connell Foundation, there was a necessity for finding funds for carrying on the research.

At that time the Director of the Biochemical Research Foundation, Franklin Institute, came to Kingston to see the work we were doing and was interested in it to the extent that he determined that he would help to finance the work and also do some work in the Biochemical Research Founda-

tion, Franklin Institute. The grant at this time was given through Doctor Ellis McDonald, Director of the Biochemical Organization, having come originally from E. I. Du Pont de Nemours, Doctor Rent, as a charitable gift.

Q. Was the affiliation of the Hendry-Connell Research Foundation, Limited, with the Biochemical Research Foundation of the Franklin Institute terminated? A. Yes, it was terminated in January, 1937.

Q. What was the reason for this termination, Doctor? A. Well, the original agreement carried with it a three-year contract under which we were to receive \$25,000 a year, and that terminated at that time, and it was felt better to disassociate the two Foundations, and that was done.

Q. Has Ensol ever been investigated by an independent group? A. Yes.

Q. Who were the members of the group and by whom were they appointed? A. The members of the group were two experts in the field in which they were expected to work and they were appointed by the Ontario Government through the Public Health Department.

They are here at the present time.

Q. What are the names of these members, Doctor? A. Doctor W. T. Connell, the same name as mine but no relation to me, and Doctor E. P. Johns.

Q. Why do you wish to obtain a patent for your invention, Doctor? A. I think it is essential to have patent protection on this type of invention from the point of view of protection of cancer patients and the general public.

69 It would not do to have a fly-by-night organization or fly-by-night people sending it all over without control.

It should be eventually placed in the hands of a competent, first-class company to handle and should be thoroughly controlled so that there could be no incident happen like the one that has already happened.

Q. How many countries have granted patent protection on your invention now in suit? A. Eighteen—I believe

eighteen. Of course, we had more patents but the countries are not there any more—Czechoslovakia, Holland, and so forth.

Q. Is it essential that you have a United States patent for this invention? A. I think it is essential for the good of the public as a whole, yes.

Mr. Connolly: The direct examination is closed.

Cross-Examination

By Mr. Mackey:

Q. In this case, the case of the Chinese patient I think it was, "Mr. SL," whose case is case No. 1 in the bulletin—That is correct? A. That is the case.

Q. You first treated him on May 10, 1935, was it not, or some such date? A. I am not prepared to say definitely from memory. If I had the case before me—
70 I know it is accurately reported there.

Q. I am merely giving the date in your bulletin. It says:

"The case was referred as hopeless on May 10, 1935. Treatment with Ensol was commenced on May 10, 1935."

Does that refresh your recollection? A. I think so.

Q. How, do you remember when he died? A. I think he died in the early part of 1936.

Q. I may refresh your recollection by referring to the post-mortem reports upon cases treated with Ensol as they appear in this record.

That may assist you? A. (after examining the document under consideration) Yes; there is a follow-up on these cases.

Yes, that is right; in November, 1935.

Q. November 10, 1935? A. Yes.

Q. The second case that you mentioned was this lady that you treated? A. Yes.

Q. Was that the second case? A. Yes; that is the second case reported in the bulletin

Q. That is case No. 2 of Mrs. E. M., aged forty-five years?

A. That is right.

71 Q. I note in that case it says that opiates were reduced to heroin, one-twelfth grain, which has since been discontinued entirely. A. Yes.

Q. That is in this report? A. Yes.

Q. But at the post-mortem I notice this statement, that pain was controlled for a time by novocain injections but the patient was very neurotic and rapidly built up a high morphine tolerance.

So, before she died, she had come back to opiates, did not she? A. I am not sure that is right. Where does that come in in the history?

Q. Again as in the post-mortem of the case, case No. 2, of Mrs. E. M. A. You mean in the follow-up?

Q. Yes, in the follow-up, yes.

I think you will find it on the next page (referring to the document heretofore identified). A. I do not think that patient received Ensol on the final—just before death.

Q. Does that sometimes happen in the Ensol treatment, that is, the patient is relieved for a time and the pain increases?

72 Have you run into that? A. I beg your pardon?

Q. Have you ever run into a situation, with Ensol treatment, where a pain may be relieved for a time and then come back again and the Ensol have no effect? A. Yes, later on in some cases; but that depends entirely on the type of growth rather than the location of the growth.

Again, pain is a difficult thing to discuss.

If you would make yourself a little more explicit, perhaps I could tell you.

Q. I am merely using the term "pain" as it is used here; that is, pain alleviation, an easement of pain", and so forth.

A. True. And would you repeat your question again?

Q. I ask you if you have had cases in which pain was relieved for a time by Ensol and then, in spite of treatment, the pain returned? A. Yes; there are some cases of that type.

Q. And also because— A. (interposing) May I—

Q. (interposing) I beg your pardon? A. That does not detract from the value of the Ensol as pain-relieving, because if you had not Ensol you would still have to have something else.

73 Q. And also because there are cases in which Ensol does not relieve the pain at any time? A. There are a few. That, of course, is common to all medicine. You do not get one hundred per cent in medicine, I don't care what type of ailment you are treating.

Q. And are there also cases in which the use of Ensol appeared to increase the pain? A. No. I think that your point there is due to a misunderstanding. Where Ensol is given and pain is a symptom and you gradually increase the dose, pain may be encountered as a local reaction in the tumor mass as the dose goes up to a certain level. If, at that point, where you have produced an increase in pain, you lower the dose slightly below that pain-producing level, then you have pain-control.

Q. Is that what you meant by this article written by you, H. C. Connell, in your bulletin No. 1, on "Clinical Results of Ensol Therapy," and I read this under the heading "Pain."

"Of the 382 cases pain was not a symptom of the disease in 88. Of the remaining 294, pain was partially or totally relieved in 279 cases, or 95 per cent. In 15, the patients complained of increased severity of pain."

A. Meaning that tumor reaction which is also manifest by a prickling or tingling sensation in the growth itself; that was one of the main symptoms that led us to believe there was something really specific and warranting careful investigation here.

74 The mere fact that you could inject something into a patient's arm and in the course of two or three hours have a prickling or tingling sensation in the region of the growth itself was evidence that something, specifically, was taking place.

The only reaction that I know of that is analogous to that at all—and I am not prepared to explain it any more than this action is explained—is the Jarish-Herkishmer reaction in the treatment of syphilis with 606. We do not know what that reaction is or why it is caused, but it does occur and it is right in the lesion.

So that was really one of the points which helped to confirm my suspicion that there was something really valuable here and that I must find out what it is if possible.

Q. Now, you have used, as I understand it from these case histories, Ensol in quite a number of cases where pain is not a symptom.

Is that true? A. Oh, yes.

Q. Now, to get to this incident of this— A. (interposing) May I say something there?

Q. Yes. A. As a cancer case progresses, if it progresses on toward its completion or toward death, I do not think there are many of them—less than one per cent—that would not have pain. Before death, as they get on to the
75 stage of obituty, they all have pain, but in the earlier stages of the final session not all of them have.

Q. Now, this product that was contaminated by the tetanus germ, was that Rex? A. That was known, I believe, from hearsay only, it was Rex.

Q. Now, I notice in your bulletin No. 2 that we have an article by William Holt, a doctor in Portland, Maine, and he gives a number of cases here of pain relief and so forth, and he says this:

“Rex is the temporary name given to Ensol made in the laboratories of the Biochemical Research Foundation of the Franklin Institute, Philadelphia, which is affiliated with the Hendry-Connell Research Foundation, Kingston.”

As I understand it, you maintain this is a different product? A. No; that work was done—May I have the date of the article?

Q. The article I do not think is dated; it is in your second volume, which is dated January, 1937. A. During the

course of our affiliation with the Biochemical Research Foundation of the Franklin Institute, which lasted till January, 1937, the Biochemical Research Foundation did supply Rex, what they called a Rex solution, to doctors as we were doing from our Foundation, but beyond our
 76 affiliation with them, how they altered their solutions and what they did to them, I absolutely have no idea, and the Florida incident occurred two months, at least, after that.

As a matter of fact, when we left the Biochemical Research Foundation to do our own research, and thought it better to separate, I heard nothing further from them with respect to reports on work or what they were doing.

Q. Now, in speaking of these cases you said you used Ensol for pain and did not know of any cancer case in which, before the end, there was not some pain suffered.

What brought that to my mind was this case of Mr. J. F., aged seventy-two— A. (interposing) Pardon me. I think you are mistaken as to what I mean there.

I meant in the untreated case, not in the Ensol-treated case.

Q. What I was getting at was this: You do use it whether pain is a symptom or not.

Is that true? A. Yes.

Q. I was referring particularly at quoting this case, a Wilmington case, in which an aged patient whose nose was operated on is considered, and I find a notation at page 108
 77 of your Volume III that Ensol was given to prevent secondary growth from coming back. A. We had the hope that it would. It was given with the idea that we might produce a prophylaxis and, as you know, that principle may have that effect.

Q. Now, I think you referred to patents you had in various foreign countries, did you not? A. Yes.

Q. Are they patents on the disclosure in this case or are they patents on the disclosure in the parent case of which this is a continuation and part? A. Since I did not draw

up this patent and do not understand that legal phraseology very well, I would like the permission of your Lordship to consult counsel if I may, and have Mr. Connolly, my lawyer, answer that, as perhaps he can.

Q. Do you recall when the applications were made for these various foreign patents? A. Yes. I cannot give you the dates offhand.

Q. Can you give the year? Were they made in 1935 or 1936 or '37? A. Yes, I think some of them were.

Q. 1935? A. Some were made in 1936; I think perhaps the first one was in 1936.

Q. I notice that this application was filed April, 1937, was it not? A. Yes, as far as I know, yes.

78 Q. In that application you made oath, did you not, and in your oath you referred to the disclosure in a then pending application in this country and referred to a list of various patents?

Do you care to read that over more carefully (handing to the witness a paper writing)?

Mr. Connolly: I believe, if I may, I can save a little time here by stating that this application is a continuation application and that it covers not only the basic invention of 1935 but the succeeding development over a period of approximately two years. The twenty-odd foreign patents issued are based solely on the basic invention. They are not as complete as this application.

Mr. Mackey: That will save some time, then.

By Mr. Mackey:

Q. I have just one more question:

Do you recall the disclosure of your basic invention in this country? A. What do you mean by "disclosure"?

Q. Do you recall when the disclosure was first made, what the disclosure was—that is, what the broad invention was?

I will give you a copy of the specification (handing a document to the witness).

I will ask you whether "pain alleviation" was mentioned.

That is, in that original disclosure? A. I do not
79 remember.

Q. You may look through it, as a matter of fact, and see if you find it.

(The witness examined the document under consideration.)

The Witness: Evidently I cannot take time to read all this over, but as far as I have gone I do not find it.

The Court: Well, counsel for the plaintiff must know.

There was no claim of pain alleviation in this original basic petition?

Mr. Connolly: No, your Honor. The original application referred, as I remember it, to just a product and the process of making that product and in the body of the disclosure I do not remember whether the cases referred to pain alleviation or not, but I do know it was not stressed.

The Court: Counsel for the Government is contending that there is no claim at all in the original basic patent for pain alleviation.

Mr. Mackey: I find none, your Honor.

By Mr. Mackey:

Q. As a matter of fact, was not that originally drawn more as a control of cataract tissue and a control of cancer tissue by causing regression in growth? A. No. It is a matter of the development or a treatment for the disease.

There is no claim for regression of tumor and
80 disappearance of the tumor mass.

Q. As I understand it, you do not claim Ensol as a cure of cancer? A. There never has been any attempt to claim Ensol as a cure for cancer.

I would like to make that clear.

Q. The sole claim is pain alleviation? A. The sole claim is pain alleviation and, naturally, anything else that goes with it.

Q. And the original case and the former patents which you have bear no mention of pain alleviation? A. May I ask my Solicitor about that? As far as I know, no.

Mr. Mackey: That is all.

Redirect Examination

By Mr. Connolly:

Q. Doctor, have you ever believed or ever represented that this invention of yours was one hundred per cent effective? A. No.

Q. In the reduction of pain? A. No.

Q. Do you know of any medicine or any method of treating a disease which is one hundred per cent effective? A. No, I do not.

Q. During your cross-examination you were
81 handed an application filed by you in 1935. Was that, Doctor, at the time you commenced this development and completed your development on the treatment of cataract, or was it at some other time? A. It was the time that the cataract work had been completed, yes.

Q. You were asked on cross-examination about the composition of this product of the Biochemical Research Foundation called Rex which was responsible for the Florida disaster.

What was the constituent of that product Rex which caused the difficulty? A. Tetanus toxin.

Q. Does Ensol contain tetanus toxin? A. Decidedly not.

Q. Is the process of manufacturing Ensol one wherein there is likelihood that the product would be contaminated with tetanus toxin? A. Not when manufactured under proper conditions and proper control.

Mr. Connolly: For the purpose of the record I should like to quote the first and I believe broadest claim from this 1935 patent application. It may make the record a little clearer.

That claim is: The method of obtaining an active substance specific for the decomposition of a given foreign

protein in the animal body comprising growing a proteolytic micro-organism on a protein of the type to be decomposed and extracting from the product of such growth a liquid containing an active substance.

82 I hand you that application, Doctor, and ask if reference is made in that claim to cancer (handing a document to the witness).

The Witness (after examining the document in question): Reference is made in this claim to cancer since cancer is a foreign protein growth in the body.

By Mr. Connolly:

Q. Is reference made in that claim to cataract tissue? A. Yes, I believe so; a cataract tissue is a foreign protein.

Q. Is reference made in that claim to cataract tissue also?

Mr. Burns: If your Honor will refer to claim No. 2 before the Court, it is set out in paragraph 8 of the complaint and sets forth substantially the identical subject matter as far as the material issues are performed.

The Witness: Yes.

Mr. Connolly: The redirect examination is closed.

Mr. Mackey: I have no further questions.

(The witness thereupon was excused and retired from the witness stand.)

The Court: You may call your next witness.

83 Thereupon **Dr. Walter Thomas Connell** was called as a witness for and in behalf of the plaintiff herein, and being then and there duly sworn by the Clerk of the Court, assumed the witness stand and, upon examination, testified as follows:

Direct Examination

By Mr. Connolly:

Q. Will you please state your full name, age, and residence, Doctor? A. Walter Thomas Connell; I am in my sixty-eighth year and I live in Kingston, Ontario.

Q. Are you any relation to the applicant of the patent application in suit, Doctor Hendry C. Connell? A. I am not.

Q. Will you describe, briefly, your education and experience? A. I was educated in the public schools and the high school and matriculated in the University, graduated in medicine in 1894. Following graduation I went to London, spending a year and a half there in post-graduate work and in the study of pathology.

On my return I was made Director of Pathology of the University, succeeding to the professorage in the following year, and held the chair until 1920, except for the war years when I was overseas, and since 1920 I have
84 been Professor of Medicine in the University at Kingston, Queens University at Kingston, with the privilege of consultation and practice.

Q. Are you a Canadian citizen? A. I am.

Q. What is your present occupation or profession? A. Consulting physician, Professor of Medicine, at Queens University.

Q. Do you belong to any professional societies? A. Our local medical society, the Provincial Society, and the Ontario Medical Association, the Canadian Medical Association, and the British Medical Association.

Q. Have you held office in any of the societies you have named? A. In our local association but not in the Provincial or others.

Q. Are you employed directly or indirectly by the Hendry-Connell Research Foundation or any member thereof? A. No, I am not and have no connection with them whatever.

Q. Are you employed by the Ontario Government or by the Minister of Public Health of the Government? A. I was appointed with Doctor Johns to investigate the question of the uses of Ensol in the treatment of cancer, starting the first of July, 1939.

Q. How long did you conduct that investigation
85 of Ensol under this appointment? A. It is still under examination and investigation.

Q. Under the auspices of what group was this investigation conducted? A. It is being conducted for the Department of Health of the Province of Ontario.

Q. What phase of this investigation are you responsible for? A. The clinical aspects of cancer treatment especially.

Q. Would you please describe briefly your investigation of the clinical aspects of this invention? A. In the clinical work we had for examination the cases actually under treatment by the Hendry-Connell Research Foundation, and the case histories of those cases which had been treated from the institution of the treatment up to the present time.

From the examination of those patients that were available and from the examination of the records that we have, we draw our conclusions from a clinical point of view.

Q. Approximately how many patients and case histories of patients treated with this invention have you investigated? A. Slightly over 1700.

Q. Based upon your investigation of those cancer patients treated with Ensol, Doctor, have you any conclusions
86 as to the approximate percentage of those cases which experienced reduction in pain as a result of this treatment? A. Might I say that pain in cancer cases depends upon a number of different reasons: it may result from a pressure of the growing growth or cancer on nerve fibers or nerve endings in the growth; it may result from the exposure of nerve endings when the growth reaches the surface of the body or one of the members of the body, like the stomach; it may result from ulceration or erosion or result in a hollow viscus due to either the obstruction of the canal of the viscus or the distension of its wall.

So the question of relief of pain depends to some extent upon the individual case and our basis of investigation was

much wider than that of pain relief only, but sooner or later in practically every case of cancer pain becomes a certainty.

There are very, very few cases of cancer that do not show pain at some time in their course.

Now, in the investigation of these case histories it was found that about roughly 65 per cent did show relief, pain relief.

Pain relief was only one of the features.

Q. What other beneficial results did you notice in those patients treated by means of this invention, Doctor? A. Other features taken into consideration were the general feeling of the patient as far as well-being was concerned, increased appetite, gaining of weight, increase of
87 better color, and all resulting in some prolongation of life.

Q. Have you ever seen any patients who were treated with this product and who were harmed as a result of this treatment? A. I can say very definitely that the use of this material is harmless; it is not harmful in any phase of it.

Q. Prior to the discovery of Ensol, how did the physician combat pain in the treatment of cancer patients, particularly those beyond the help of x-ray, radium and surgery? A. Well, we were left, if they were beyond treatment with surgery, x-ray, or radium, we were left to the use of sedatives particularly, of course, morphia and its like substances, morphia, heroin, codine, and so forth.

Q. Did the use of sedatives for this purpose have any disadvantages, Doctor? A. In the majority of cases you simply have to increase the dose to get the effect. One creates a tolerance for these substances.

Furthermore, those drugs also have an effect other than that of pain relief. They have effects like upset stomach, give rise to constipation, and other features that are objectionable. But we have to use them sometimes for pain relief despite their objectionable features.

Q. For how many years have you been interested in the study and treatment of cancer? A. Practically since graduation.

88 Q. And, again, what was the year of that, Doctor?
A. 1894; forty-seven years this spring.

Q. As a result of this investigation, Doctor, and the number of years you have been interested in this subject, is it your opinion that this product which alleviates or reduces pain in approximately 65 per cent of cancer cases treated is a valuable contribution to the medical practitioner? A. I consider it as such as a result of my investigation.

Q. Would you or would you not as a result of this investigation recommend the use of this product in conjunction with x-ray, radium, or surgery in the treatment of cancer patients? A. As the material has proven itself to be harmless and as it has certain effects in alleviating symptoms, reducing pain, increasing well-being, prolonging life, I certainly would consider it advisable to use it.

Q. Would you recommend Ensol for those purposes, Doctor, if you had any doubt as to its harmlessness? A. I certainly would not if I thought it in any way harmful. If I thought it in any way harmful I would not recommend its use.

Q. Would you recommend Ensol for this purpose if you had any doubt as to its efficacy? A. No, I certainly would not recommend it if I had.

Q. Doctor, do you believe it is possible to determine the pain-reducing properties of a product by an investigation conducted on rats, mice, rabbits, or other
89 animals? A. I do not know any way we can estimate pain sensed by these animals or to register whether or not they get relief.

Q. Do you know of any medicine or method of treating diseases which is one hundred per cent effective, Doctor?
A. No; I regret to say I do not.

Q. Would you consider that an average of approximately 65 per cent benefication is a high average? A. It is a good average.

Mr. Connolly: The direct examination is closed.

Cross-Examination

By Mr. Mackey:

Q. As I understood it, in your testimony and discussion of what causes pain, would you say that the relief of pain in these cases would be due to retrogression of the tumor, reducing the size of the tumor? A. That would relieve the pain where the pain was due to the tension or pressure of the growth on nerve fibers or nerve endings. It would not relieve the pain where there was exposed nerve endings on an ulcerated surface or a hollow viscus due to either the obstruction of the canal of the viscus or to distension of its walls.

Q. Now, you have spent a good many years, as I understand it, in the treatment of cancer cases and in the investigation thereof.

90 Do you recall ever investigating any of the other substances, such as the use of magnesium sulphate or Epsom salts for the relief of pain as referred to by Shaw? A. I have not investigated, but one looks to the literature, not to the cancer clinics, for their opinion upon them before adopting procedures.

Q. What is the opinion you have arrived at on those products from your study of the literature? A. I cannot find it is being adopted by any of the cancer clinics in the treatment.

Q. Would the same apply to the Coffey and Humber gland extract? A. Yes, sir.

Q. To your knowledge? A. Yes, as far as my knowledge of the literature is concerned.

Mr. Mackey: Thank you. That is all.

By the Court:

Q. Will you tell the Court about how the Ensol affects the nerves or the nervous system of a person suffering from the cancer? A. My idea, sir, is the relief of pain is a definite, difficult thing to explain in any particular case, but my idea is in the cancer cases where there is a reduction in growth pressure, the growth pressure is what presses on nerve fibers and nerve endings, and if that tension is eased pain is also relieved in that manner.

Q. Is it your opinion that this Ensol decreases the growth of the cancer? A. That is one of our findings; there is lessening in certain cases, apparent cessation of growth at times and, at times, definite.

Q. How does it get into the cancer? A. Through the bloodstream; it is given by hypodermic injection.

Q. And your idea is that this reduction of pain is just a secondary result? A. It is one of the results.

Q. Secondary. The result, as you say, of the use of Ensol is that it decreases the cancerous growth? A. That is one theory of its action and the more reasonable theory in cases that give relief is that by holding up the growth and pressure on nerve endings because of that growth that we get relief.

Q. But you do not claim the nerves or nerve fibers of the body go into the cancerous growth? A. Pardon me?

Q. The cancerous growth is a second growth that feeds on the body? A. It is a second growth that feeds on the body but it originates from body cells, body tissue; it is not a new substance—very old.

Q. That is your theory? A. No, it is a fact.

Q. Your only idea about the way to get any relief from pain is that there is a shrinkage or a narrowing of the cancer's growth and that relieves some pressure on the nerve? A. But it acts in a different manner from morphine which acts on the centers that register pain in the brain. This acts purely in a different manner.

Q. It acts on the cancerous growth and it causes that to shrink and you say there is less pressure around it? A. And in them. The nerve fibers, the tissue, is infiltrated—I will explain it this way: if you have a growth into the tissue—

Q. (interposing) You do not want to tell the Court that the nerves grow into the cancer? A. No, but they are more resistant to the infiltration of the tumor than other tissue. If so, they are entangled in the growth and become subject to the pressure.

(The witness thereupon was excused and retired
93 from the witness stand.)

The Court: I wanted to ask the preceding witness, the inventor, one or two further questions.

Mr. Connolly: Yes.

By the Court:

Q. Have you obtained a patent on this invention in Canada? A. Yes.

Q. On this one—I don't mean the prior one.

Mr. Burns: The patent in Canada covers this plus the treatment of cataracts; that is, these are not independent inventions, but this is merely a moving forward of the old one.

The Court: I want to know whether the first witness claims to have received and has received a patent on this Ensol as a pain-alleviator.

Mr. Burns: The patent covers the product. It is not limited to pain alleviation.

The Court: It does not cover pain alleviation.

Mr. Burns: Of course, covering the product covers all uses of the product.

The Court: That is not in one of the claims.

Mr. Burns: It is not in one of the claims, your Honor.

• • • • •

98 **Dr. Walter Thomas Connell** a witness heretofore called, sworn, and examined on behalf of the plaintiff, resumed the witness stand and upon further examination testified as follows:

Direct Examination (resumed)

By Mr. Connolly:

Q. Will you make the statement that you wish to the Court, please, Doctor Connell? A. Your Honor, I expressed to the counsel this morning my belief that I had left the impression on your mind that my only explanation for the relief of pain in cancer cases treated by Ensol was through cessation of growth and shrinkage of the mass.

99 That explanation will account for certain of the cases but it does not, in any way, account for many of the cases in which pain relief was evidenced.

The cessation of growth would account for that in certain of the cases, but in certain of those cases in which pain relief was obtained there was no cessation of growth as measured over days or weeks, and yet pain was relieved, so that explanation would not hold.

I have no theory which will explain entirely or in all cases the cessation of pain, but we have found that as in the records examined of the 1,700 cases and in the cases that I have seen under treatment at the Foundation Clinic in 65 per cent roughly, or approximately, of the cases so treated, and that along with other evidences of clinical improvement.

That is the point, sir.

By the Court:

Q. Then you claim this Ensol had some effect upon the nerves or nervous system in the body in and around where the cancer is working? A. In some way not explained, simply by tension and pressure.

Q. Then you would say it acts like a sedative or narcotic? A. It acts in the manner which approximates that of

100 a sedative, but whether exactly like a sedative I could not say. I have no theory.

I would have to consider each individual case to give an explanation, but I would have to surmise that theory; I could not prove it.

Q. You do not know the chemical contents of this Ensol?

A. No, I do not, except that it is an antigen substance.

Mr. Connolly: May I ask one question there, your Honor?

The Court: Yes.

By Mr. Connolly:

Q. I would like to ask you, Doctor W. T. Connell, whether when you stated this acted in certain respects like a sedative you meant that its physiological action was similar to that of a sedative or merely its result on pain? A. The result on pain, not its exact method of action. Each sedative differs a little in its method of producing or reducing pain cessation in its physiological action.

Mr. Connolly: Thank you.

Mr. Mackey: I have no further questions:

(The witness was again excused and retired from the witness stand.)

101 Thereupon **Dr. Eugene Percy Johns** was called as a witness for and on behalf of the plaintiff herein, and being then and there duly sworn by the Clerk of the Court, assumed the witness stand and upon examination testified as follows:

Direct Examination

By Mr. Connolly:

Q. Doctor Johns, will you please state your age and residence? A. I am approximately forty-one years old and live in Kingston, Ontario.

Q. Will you describe briefly your education and experience? A. I received my primary education in the public schools of Windsor, Ontario; my high school education partly in Windsor, Ontario, and in St. Thomas.

Following my graduation from high school I entered the University of Western Ontario as a medical student and graduated in 1926; I tried the medical council examination, obtaining the degree of Licentiate of the Medical Council of Canada; following graduation I entered the Faculty of Medicine of the University of Western Ontario in the department of pathology, after a year's general internship in the General Hospital. I stayed there two years and transferred to the Faculty of Public Health in the same university, in the department of bacteriology and pathology, and I have been there ever since.

At the present time I am holding the position of chief of the department of pathology and bacteriology on the Faculty of Public Health, assistant professor of pathology in the Faculty of Medicine, and pathologist to the Ontario Hospital at London.

Q. What, if any, professional societies are you a member of? A. I belong to the local medical society in Kingston, the local medical society in London, Ontario; the Provincial and the Canadian Medical Associations.

Q. Are you a Canadian citizen? A. Yes, sir.

Q. Are you employed directly or indirectly by the inventor, Doctor Hendry C. Connell, or by his Research Foundation, or any member thereof? A. No, sir.

Q. What is your present occupation, Doctor? A. At the present time I am on loan from the University of Western Ontario to the Ontario Department of Health to conduct research work in connection with Ensol.

Q. By whom were you delegated to conduct this research work? A. The Minister of Public Health, the Honorable Mr. H. J. Kirby.

103 Q. What was the date of this appointment by the Minister of Public Health? A. July 1, 1939.

Q. Were you appointed alone to conduct this investigation? A. No, sir.

Q. Who else was appointed? A. Doctor W. T. Connell and myself were appointed to conduct the investigation, Doctor W. T. Connell to investigate in the field of clinical

research, myself to conduct experiments in the field of laboratory research.

Q. What is the personnel of the staff which you use in conducting this investigation? A. A laboratory was established in Kingston, in the Ontario Government Building, entirely separate from the Connell Research Foundation. The staff consists of myself and six workers, including a serologist and an assistant serologist, a chemist, a stenographer, and laboratory assistants.

Q. How long has this investigation of the invention here in issue continued, Doctor? A. Of our investigation, do you mean?

Q. Yes. A. It has not been completed; it has been in progress since the first of July, 1939, and is still in progress.

Q. Were you authorized to attend and testify in
104 this suit by any official of the Ontario Government?

A. Yes, sir.

Q. Have you any written authorization to that effect, Doctor? A. Yes, I have.

Q. I hand you a letter on the stationery of the Minister of Health, Interior Parliament Building, Toronto, dated January 14, 1941, addressed to Doctor E. P. Johns, Ontario Government Building, Barrie Street, Kingston, Ontario, and signed Harold J. Kirby, Minister of Health.

Is that the letter to which you refer, Doctor (handing a paper writing to the witness)? A. (After examining the document last referred to) Yes, sir.

Q. For the purposes of the record and since I understand that you want to keep this letter in your personal file, will you kindly read it into the record? A. This letter is addressed to Doctor E. P. Johns, Ontario Government Building, Barrie Street, Kingston, Ontario, under the date of January 14, 1941, re giving evidence at Washington, patent suits re Ensol.

“Dear Dr. Johns:

“Replying to your letter of January 13, and having in mind all the circumstances, I would be grateful if

105 Dr. W. T. Connell and yourself would cooperate by attending this hearing as requested by Dr. Hendry C. Connell and Mr. Connolly. I have every confidence in the judgment of this department's two representatives and will leave the matter of the evidence based on your findings as presented at this hearing entirely in your hands. Yours sincerely, Harold J. Kirby, Minister of Health."

Q. Doctor Johns, you have been present and heard the testimony in this suit of Doctor W. T. Connell.

Do you or do you not agree with his conclusions as expressed therein concerning the efficacy of this invention in the treatment of cancer? A. I do.

Q. Based upon your experience in this field and your study of this invention, do you believe that a product which is capable of reducing pain in approximately 65 per cent of the cancer cases treated is a valuable contribution to the medical practitioner? A. Unquestionably.

Q. I beg your pardon? A. Unquestionably it is.

Q. Would you or would you not recommend the use of this product in the treatment of cancer in conjunction with x-ray, radium, or surgery? A. I would.

106 Q. Would you recommend the use of this product for that purpose if you had any doubts as to its harmlessness? A. No; under no consideration.

Q. Would you recommend the use of this product for that purpose if you had any doubts as to its efficacy? A. No.

Q. Doctor Johns, do you believe that a determination of the pain-producing properties of a product might be ascertained by means of tests on animals? A. Would you mind repeating that question?

Mr. Connolly: Will you read the question, please?

The Reporter (reading):

"Q. Doctor Johns, do you believe that a determination of the pain-reducing properties of a product might be ascertained by means of tests on animals?"

The Witness: I do not think that you can determine pain-relief in animals. I think that you are probably referring to tumors in animals, and during the course of the last ten or twelve years I have seen probably thousands of spontaneous and transplantable tumors in animals, and I know of no way that you can tell whether the presence of that tumor is causing pain in the animal.

These animals will have tumors. They get pretty large. I have seen tumors whose bulk would be perhaps more than the whole of the animal when the tumor is removed, and yet these animals with the tumors will be running around
107 in the cage with the rest of the normal mice, apparently enjoying themselves, eating, drinking, carrying on, and carrying on apparently a normal mouse-existence.

They cannot talk to you.

The only method of estimating it is by subjective symptoms, and I have never seen any subjective symptoms which would lead you to believe that they did have pain or that there might be any relief from pain.

Q. Are you familiar with the published articles of Gye, Rusch and Preston, Pommerenke, and Goldfeder, referred to in the defendant's answer and I believe in evidence as Defendant's Exhibits B, C, D, and E? A. Yes, sir. One of the first things that was necessary when we started this investigation was to review the literature which had accumulated with regard to the use of Ensol and we had, of course, to take into consideration literature which was confirmatory or otherwise.

Q. Did these articles have any bearing on the question of pain reduction in cancer? A. I do not see where they have any bearing on that question at all, sir.

As I have said, I do not know of any way in which you can assess pain in animals and how these experiments would be of value in that connection I just cannot see it, sir.

Q. What, if any, conclusions have you as to the
108 value of these articles individually and collectively in determining the efficacy of this invention in the

treatment of cancer? A. We, when we commenced this work, of course we had to take into consideration, as I say, other published articles, and we had to assess them at their—as to what we considered their meaning in regard to our own research. I do not feel that they have very much bearing on the problems that we have to undertake. The reason for that statement was that, there were probably several, the most important probably was the fact that we had available to us a large number of clinical records present in the files of the Foundation; there were approximately 1,700 or 1,800 of these records; they were collected from a cross-section of the country by some hundreds of physicians and our review of these records definitely indicated that in at least two-thirds of the cases definite advantages were gained by the use of Ensol including, of course, relief from pain.

Those cases were the experiments, the human experiments, if you will. They were conducted on humans, on humans who were suffering from spontaneous tumors, tumors which arose in the individual; many of them were in cases who had exhausted any recognized or other method of therapy, including surgery, x-ray and radium and, as I say, they did show very definite benefits.

On the other hand, you have the investigations by Gye, Pommerenke, Rusch, and Preston, and Goldfeder, 109 who were working on animals and whose results were essentially negative according to their conclusions.

Personally, we prefer to believe the evidence which was given by a large number of investigators on a large series of cases rather than the evidence presented by four investigators on a comparatively small series of animals.

I do not suppose—I do not know, offhand, but I doubt very much whether in all of those investigations more than 100 animals were used.

There must, of course, be some reasons for such discrepancy, and I think the second reason for questioning the validity of these articles or the validity of the conclusion, lies in the fact that those articles were done, three of them

at least; in 1935 with Gye; Pommmerenke, and Rusch and Preston were in 1936—those articles were done in the early part of this work and at that time it was considered that Ensol acted by means of a specific enzyme which contemplates that the action of the substance which you are using is directly on the tumor and you would expect fairly immediate effects on the tumor.

When we entered this picture, the enzymetic theory had practically been discarded and the theory which was involved was the antigen antibody theory, meaning that you were innoculating something into the individual which would not act directly on the tumor but would stimulate in that individual the development of substances which would secondarily affect the tumor.

110 Now, you cannot get the development of antibodies in a matter of days.

Take, for instance, if you please, in the development of immunity against diphtheria. Of course, the innocations in that process last over a period of three weeks, and you do not expect to get the maximum results from your innocations until probably three months after, or until three months have passed.

In transplantable tumors in animals you are innoculating a tumor from one animal into another. The host into which you innoculate that tumor must be such that the tumor will grow and it has been my experience that these tumors do grow when they are innoculated into susceptible hosts with considerable rapidity. Using susceptible animals you can expect to get that tumor graft to make itself apparent probably in a week or ten days. You cannot use that tumor animal until that period has gone because you do not know whether your graft is going to "take."

From the time that you make your innoculation until the animal dies of its tumor usually is a period of a month or five or six weeks. In that length of time you have not time for the animal to develop any antibodies and you naturally cannot expect to get any influence on the growth, so that I do not think that on the basis of an antigen antibody theory

that these negative results in any way rule out the results which we obtained clinically.

111 Would that answer your question?

Q. Does that answer apply to all four of these articles, Doctor? A. Yes. According to my recollection all of these articles were done on transplantable tumors in animals, mice, rats, and rabbits.

I do not think—I am quite sure none of them used spontaneous tumors and, of course, there is a difference between a spontaneous tumor and a transplantable tumor.

The spontaneous tumor is one which arises in the individual who has the cancer; it rises from his own cells. The transplantable tumor is one which arises or may have arisen years back in some other animal and has been transferred through successive generations and some of those tumors at the present time are ten or fifteen years old, transferred through susceptible animals, and the original tumor being ten or fifteen years old.

Q. Which type of cancer is the human cancer, Doctor? Is it the spontaneous or the transplantable? A. The spontaneous tumor; you just do not get the transplantable tumor in humans.

Q. Is this antigen antibody theory to which you refer one that is the result of the investigation by this commission or is it just another nice figment of the imagination? A. No; it has been developed as a result of this investigation.

112 The results of the Foundation disclosed, our examination of them disclosed, that they had antigenic substances in Ensol and that they could demonstrate the presence of antibodies in cancer patients who had been treated with Ensol, using the Ensol as an antigen in subsequent serological tests.

We have confirmed that result in our own laboratory, and we have established that these antibodies do not occur in cancer patients who are not treated with Ensol; they do not occur in normal individuals and they do not occur in individuals suffering from diseases other than cancer who have not been treated.

We have been able to produce these antibodies in normal individuals.

Q. Are there any well-known treatments, Doctor, which are based upon this antigen antibody phenomenon? A. Oh, yes.

Q. Will you please describe for the purposes of the record a few of them, just referring to them; not in detail? A. Such diseases as diphtheria, tetanus, scarlet fever, they are just among the more common examples of its use.

It might be used, of course, in one of two ways: firstly, to build up an immunity, prophylactically, against a subsequent infection, or it may be used prophylactically by the use of pre-formed antibodies which can be used when a patient has the disease.

113 It is a well-recognized method of treatment.

Q. As a result of your investigation of this invention, Doctor, do you believe in the approximately 65 per cent of the cancer patients treated with it who experienced pain reduction, that this reduction in pain was due to a regression of the malignancy? A. No, I do not think you can make that statement at all.

Unquestionably, relief from pain may be associated with the regression of tumor growth, but in our review of these records many of them show no regression of tumor growth; in some of them there was even an increase. As a matter of fact, many of them went on and died with cancer and yet even in those individuals there was definite clinical improvement with relief from pain.

Q. Have you, then, any idea as to why this reduction in pain is accomplished in all these cases by means of this treatment? A. I have no theory to explain it. I am sorry I cannot explain that.

Mr. Connally: Your witness.

Cross-examination

By Mr. Mackey:

Q. In your investigation, just what did your studies
114 include?

Did you personally examine cases or read the records of cases? A. Doctor Connell and myself reviewed all of the records which were available at the Foundation, in their file. In addition, there were a certain number of patients who were coming into the Foundation, and those patients I saw personally.

Q. Now, in your study—Had you finished your answer?

A. Yes.

Q. In your study of the literature and these writings of Gye, Rusch and Preston, Pommerenke, and Goldfeder, did you run across any other articles by any other investigators who had obtained negative results? A. I think those were the main ones.

Q. Do you recall any articles by a man named Ettinger?

A. Oh, yes; those experiments were done in Kingston.

Q. And I will read to you a paragraph found in Plaintiff's Exhibit No. 3, at page 78 where this is said:

"I am not satisfied, however, that it has been proven that cancer Ensol does not contain toxin. The existence of toxin infiltrates from cultures of histolyticus is described in textbooks on bacteriology. This toxin is produced quickly, is destroyed quickly, and may be removed by a process which involved prolonged infiltration. Toxin produced by growth on cancer cells might therefore have been destroyed
115 or removed from the material which I introduced into mice some time ago. The fact that patients experienced no toxic effects may be due to the small doses given."

I ask you whether you agree with that statement or not.

A. On the textbooks, he is perfectly correct when he states that the textbooks in bacteriology have described toxic products produced by histolyticus; on the other hand I can say we have grown proteolytic histolyticus and we have not been able to demonstrate any toxins.

Another phase of our investigation was the inoculation of Ensol into a group of entirely normal patients, extending over a period of twenty to thirty inoculations in a group of

about seventy patients. There was none of those patients who experienced any deleterious effects whatever with the exception of a transitory reaction at the site of inoculation, where the material was inoculated. It became a bit swollen, reddened, and a bit hot at the feel. That subsided within a day or so and it is the type of reaction which you may expect from any inoculation of the amount that we gave.

Q. Then, as I understand your testimony, whereas Ettlinger says he is not satisfied it is not toxic, you are from your investigation satisfied that Ensol is not toxic? A. I am perfectly satisfied that Ensol is harmless and contains no toxin.

116 Q. You mentioned something about animal tumors may not be affected within the time the animal dies, six weeks. A. Yes.

Q. I notice in the first case, the case of the Chinese patient, that it is reported that the Ensol was first given on May 10, 1935, and the dose was set at two c. c.'s; after ten days' treatment there was bulging and the eyelids showed some skin wrinkled.

Would you not say from that that the effect had taken place within ten days? A. I do not know why you get this variation in clinical results. I cannot explain that. That certainly does not seem to be a long enough time to develop antibodies and, too, there was some considerable variation in the alleviation of symptoms; some of them occurred very rapidly; others were delayed.

It has been our observation, however, that patients who did experience relief, who received beneficial results, were those who did develop antibodies.

Q. Now, pain relief, as referred to by you, about how fast would that take place in the ordinary case where pain was relieved? A. I do not know. It varies. When your improvement came on—that varied; sometimes it might be fairly rapidly and other times it might be three or four weeks.

117 Mr. Mackey: That is all.

By the Court:

Q. In your statement did I understand you to say that this Ensol had been tried upon healthy, normal people?

A. That is right, sir.

Q. And do you know what the result was? A. Yes, sir; I personally conducted that experiment and gave the inoculation.

Q. What was the result? A. There was no result, as far as the patients were concerned. They continued to lead a normal existence, but they did develop antibodies.

That experiment was conducted to convince Doctor Connell and myself of the harmlessness of the material and to demonstrate whether normal individuals would respond with the production of antibodies.

Q. It did not give any of them a cancer? A. Oh, absolutely not.

Q. You say they responded, showing antibodies in their blood? A. In their blood stream.

Q. Is it known what the antibodies are that fight cancer? A. No, I do not think it is definitely known.

Q. Then you cannot say that the antibodies you
118 found in these normal people were antibodies that would oppose or offset cancer?

Can you say that? A. Not definitely, but the theory is that your antibody reaction, that entire mechanism of that is to produce antibodies which will specifically act against the antigen which led to their existence.

Q. Did you use this Ensol on animals of any kind that were normal? A. That were normal?

Q. Yes. A. Those experiments are in progress at the present time.

Q. You have not done it? A. Yes, we have done it.

Q. Have you had any antibodies in them? A. Yes, we have produced antibodies in them.

Q. And, after that happened, did you try to inoculate them or transplant cancer with them? A. That experiment is one in progress at the present time.

Q. You cannot say anything about the results of such an experiment? A. It has not been going long enough, sir.

Q. You likened this to diphtheria antitoxin, did you not? A. I used diphtheria antitoxin to explain.

Q. And tetanus? A. Yes.

Q. Well, now, are not all of those methods used to fight known germs in the human system? A. That is correct.

Q. Well, now, cancer has not been classified as a germ disease or a bacillus, has it? A. No.

Q. It is just the other way? A. When I said they were used to fight known germs, they are; but it is the product of those germs which the antibody fights. The germ produces the toxin and the antibody fights against that toxin.

Q. The latest investigations of scientists and medical men do not lead to the conclusion or opinion that cancer is the result of germs or bacilli. It is an embryonic cell feeding with great vitality on the human tissue? A. That is right, but, sir, if I may say, the antigen itself—you may have an antigen; any protein may act as an antigen, and so do other cells.

Q. You are just using typical cases, just by analogy? A. Yes, sir; that is all; I would not for a minute subscribe to the theory that cancer is a germ disease or anything like that.

120 *Redirect Examination*

By Mr. Connolly:

Q. Just a minute, please, Doctor:

During your cross-examination you referred to the work carried on by you and Doctor Connell, or the investigation undertaken by the two of you.

To which Doctor Connell did you refer? A. Doctor W. T. Connell, who is my associate in this work; Doctor W. T. Connell doing the clinical work with myself in the laboratory.

Q. Do you know whether at the time Doctor Ettinger conducted the experiment which you discussed in your cross-examination Ensol was believed to be enzymetic in its action? A. Yes, it was.

Q. And would you expect pain reduction in those patients that experienced both pain reduction and regression of malignancy under Ensol treatment to take place before or after regression of the malignancy? A. Will you read that?

Mr. Connolly: Mr. Reporter, will you read the question? The Reporter (reading):

“Q. And would you expect pain reduction in those patients that experienced both pain reduction and regression of malignancy under Ensol treatment to take place before or after regression of the malignancy?”

121 A. Well, it might take place before regression or it might take place after regression.

There may be no regression and still a patient have pain relief.

Q. I refer in that question, Doctor, to that particular group of patients that experienced both pain reduction and regression.

There is a group that experienced both those symptoms and there is another group that experienced pain reduction without regression and even with increase in size.

I am referring to the first group. A. I would expect pain relief to coincide fairly well with regression of the tumor.

Q. Does anyone know what causes cancer, Doctor? A. I do not think so; I certainly do not know of anyone who knows what causes it.

By Mr. Mackey:

Q. In cancer cases that are not treated with Ensol is it not true that sometimes the tumor regresses for a while? A. Yes, I think that is true.

Mr. Mackey: Thank you.

By the Court:

Q. Sometimes it walls itself off? A. Not the malignant tumor.

122 Q. Well, not when it has progressed, but in its incipency does not Nature sometimes wall them off?

A. Yes.

Q. Calcify around them? A. Yes.

Q. And on the face of it, it is walled off? A. Yes. Unquestionably there is in the human race a very definite resisting factor in individuals; if there were not I hesitate to think how many of us would have malignancy.

By Mr. Connolly:

Q. Are the instances of spontaneous regression common or rare? A. The instances of spontaneous regression are extremely rare; they are a medical curiosity.

Mr. Connolly: Thank you.

Thereupon **Doctor Robert Norton Irwin** was called as a witness for and on behalf of the plaintiff herein, and being then and there duly sworn by the Clerk of the Court, assumed the witness stand and upon examination testified as follows:

123 *Direct Examination*

By Mr. Connolly:

Q. Doctor, please state your age and residence. A. Age forty; residence Toronto, Ontario.

Q. Are you a Canadian citizen? A. I am.

Q. Will you describe briefly your education and experience? A. I am a graduate in medicine of Queens University, having graduated in 1926; Licentiate to the Medical Council of Canada; one year's internship, General Hospital, Elizabeth, New Jersey; licensed to practice medicine in the state of New Jersey.

Until 1930 I was in general practice at Parry Sound, Ontario, starting in private general medical practice in Toronto in 1930, and I have been there up to the present time.

Q. Do I understand, Doctor, that since 1930 you have been engaged in the general practice of medicine in Toronto? A. Yes.

Q. During the course of your general practice of medicine have you had occasion, Doctor, to treat cancer patients?

A. I think the most trying cases the general practitioner or the family doctor has to deal with are the terminal cancer sufferers who are, invariably, brought back in his lap after

the specialists have exhausted their known methods
124 of treatment. It then resolves to the family doctor

as to what he can offer to do for the mother, father, or child who is ever suffering from the disease after those other methods have been exhausted.

Q. Approximately how many cancer cases have you personally treated during this general practice about which you have testified? A. I would say approximately twenty-four.

Q. What was the manner of treating cancer patients prior to the discovery of the invention here in suit? A. When the patient would come in and you are able to make a diagnosis of cancer, they were referred on to the surgeon for operation. If he could do anything for them he did. From there they were passed on to the x-ray man or radiologist for further treatment. Then back to the general practitioner.

If there was no relief that could be obtained by those patients through the methods which they had given them, you had nothing more to do for them except condemn them to a life of morphine. You could use that in increased dosages depending on the severity of their pain, get what relief you could for them from that pain, combine them with other drugs as their tolerance built up, and there was nothing more the general man could do.

One of the most trying things of any practice is to have to see these patients day in and day out with only
 125 opiates and sedatives at your disposal to treat them.

Q. Are you familiar with the invention here in suit? A. I am.

Q. When did you first use this invention in the treatment of your cancer patients? A. I attended clinics at the General Hospital in Kingston in 1935 and 1936 when Doctor Connell announced his discovery.

In 1937 I was requested to use Ensol on a private patient in the Toronto General Hospital. It was one of the worst tragedies you could see: A woman had been operated on, pronounced incurable, unoperable at least, confined to lying in bed and with not enough strength to raise her arm, being fed through the means of a nasal catheter, milk being dropped in the back of her throat; the abdominal incision broken open and she too weak to go to the operating room to sew it up.

Her husband requested Ensol treatment. After careful consideration I refused to use Ensol on the woman as I considered she was so close to termination that if it were used and she died the Ensol would be blamed for her death. Yet the husband insisted, and those things were explained to him, and it was agreed that it be tried.

In three weeks that woman was able to travel from Toronto to Kingston, a distance of 172 miles, by ambulance.

Further treatment at Kingston, under Ensol, was had. I spoke to her on the telephone from the railroad station and she was passing on back home feeling very,
 126 very well.

That fall she died, suddenly, at the dinner table, from a cerebral hemorrhage.

That was my first experience with Ensol.

Q. Do you consider that that patient was benefited by the administration of Ensol? A. There is absolutely no other way that you could explain a person picking up the way she did, getting back on her feet. It was the only treatment employed.

Q. Was that one of the patients who had pain as a symptom? A. I would say "no."

Q. She had no pain? A. She had no pain as a symptom.

Q. How many of your cancer patients have you treated with Ensol? A. I have treated with Ensol eighteen cancer patients.

Q. In approximately what percentage of those patients was pain a symptom? A. I would say of the eighteen pain was definitely a symptom in fourteen.

Q. Fourteen? A. Yes.

Q. In what percentage of the fourteen who had pain as a symptom was there a reduction in this pain due to Ensol treatment? A. Definitely in twelve.

127 Q. In the treatment of your cancer cases with Ensol, have you ever noticed any harmful effects? A. I have not.

Q. Is it your opinion that Ensol has been of benefit to these patients? A. It is my well-considered opinion that Ensol is a weapon that is being placed in the hands of the family doctor which will give him something to use on those patients which has been the greatest advance we have ever had from the medical practitioner's standpoint in the treatment of cancer.

Q. Approximately how many injections of Ensol have you made into your patient? A. I have used between 850 and 950 injections of Ensol in the treatment of patients.

Q. Over what period of time? A. That is from 1937 until the present.

Q. Will you please describe briefly the condition of just a representative few of these patients who suffered pain, before and during the administration of Ensol? A. The case that comes to my mind first comes because the man was inoperable, suffering from cancer of the prostate. He was suffering severe pain in the rectum, unable to pass urine, though not totally obstructed.

The expectancy of that man was put down by the
128 bladder specialists as six weeks.

We started him off on Ensol. The first noticeable improvement was within four days, of definite pain reduction. Going into the second week, the urinary symptoms cleared a bit, his appetite improved, he gained in weight, and he lived for eighteen months.

Now, with him the consultation with the bladder specialists definitely showed a regression in that tumor mass, although you could feel it by examining through the man's rectum, and at the time of death the mass was one-third of its original size.

There was no apparent reduction in the size of that mass until that man was on treatment some four months. His pain alleviation was apparent the first week of treatment.

That, incidentally, is the only case that I could definitely say that there was tumor reduction in. The mass was there; you could examine it and feel it and estimate its size.

Q. Will you please describe one or two other cases, Doctor? A. There was another case I had:

The woman had had her breast removed; the growth had gone to the second breast and the surgeons decided not to put her through any more surgery; the x-ray men decided she was beyond any help they could give.

129 She was in bed, suffering extreme pain, loss of weight, and loss of appetite.

She was put on Ensol treatment. Her pain cleared; she increased in weight; the ulceration of the breast healed, and the woman was able to return to visit her folks in Ireland for the period of one year.

She returned to Toronto in a very advanced stage of her disease: her breast had broken down and ulcerated. The ship's surgeon came through to Toronto with her and she was put in the hospital that way, and at that time received upwards of three grains of morphine a day.

On Ensol, which was started right away for the remaining fifteen or sixteen days of her life, we were able to definitely reduce the amount of opiates that she was getting.

Q. Excuse me, Doctor. Will you please state, for the purposes of the record, what sedative that patient was re-

ceiving prior to her trip to Ireland, prior to the time you commenced Ensol therapy? A. The sedatives would be morphine, pantopon, nembutal, sodium nembutal—whatever group of sedatives you have at your disposal; you mix them and use them to tide the patient over as far as possible.

Q. Also the amount of sedatives that that patient was receiving both before and after this trip was considered?

A. The amounts varied. One person will build up a terrific tolerance to opiates, but the amount Mrs. Cook was
130 receiving when she returned from Ireland was certainly a fair dosage; but you could give her more if necessary. But, with Ensol we were able to reduce the amount of opiates she was getting.

Q. Doctor, in the cases of the remaining patients whom you treated with Ensol and who had pain as a symptom, were they generally receiving opiates prior to the time you commenced this Ensol therapy? A. I would say yes.

Q. Were you enabled by means of this Ensol treatment to reduce the amount of opiates they were receiving? A. I can definitely say I have reduced opiates to the point where they were discontinued entirely, and I recall patients that were reduced from one and a half grains of morphine a day, where you could tide them along with nothing but aspirin and keep that up until death, and opiates and heavy sedatives were not required in that period.

Q. In how many of those patients were you able to reduce the amount of opiates they were receiving, by means of Ensol treatment? A. Well, in the twelve cases where pain was a definite symptom, just to say whether they were all receiving opiates or what amount, I cannot do that.

The question has to be answered that in that series of cases we were able to get them on a drug which was
131 not in the opiate class, if they had been taking opiates before that.

Q. Over what period of time were you able to reduce this pain in these patients by means of Ensol administration?

A. If you get a reduction of pain, that reduction will remain until the patient either expires, or if they continue to improve, they still have pain reduction.

Q. Did the pain disappear entirely in any of these patients under Ensol administration? A. Definitely yes.

Q. Do you know of any other means of accomplishing comparable results? A. I do not.

Q. Do you, as a practicing physician, consider that a product which will reduce pain in approximately two-thirds of the cancer patients, is a valuable contribution to the medical profession? A. A product that will reduce pain in two-thirds of the cancer sufferers is the most valuable addition to cancer therapy that the general practitioner has ever had.

Q. Have you noticed any other beneficial effects in the use of this material? A. Definitely: The prolongation of life, the feeling of well being, better color, the increased appetite, and a certain percentage of tumor regression, a certain small percentage of tumor regression.

Q. Did some of the cases which you treated with
132 Ensol apparently show no beneficial results whatsoever from this treatment? A. Yes, they did.

Q. How many of the cases, Doctor, out of those that you treated with Ensol apparently showed no beneficial results from the treatment? A. Out of my eighteen, I would definitely say two absolutely showed no results; definitely two showed absolutely no results at all.

Q. And were those two harmed in any way by this Ensol administration? A. No.

Q. Have you ever used Ensol in conjunction with x-ray, radium, or surgery, in the treatment of cancer? A. Before I would use Ensol in the treatment of cancer I would exhaust the other known methods of therapy and then use Ensol in conjunction with them.

Q. Have you ever done that, Doctor? A. In all my cases that would be done.

Q. Have you ever used Ensol at the same time your patient was undergoing x-ray, radium or surgical therapy?

A. Yes.

Q. Was it beneficial in those cases? A. The benefit was —the credit for the benefit might either be taken by the x-ray, surgery, or Ensol; it is very, very hard to
133 evaluate the benefit in a series where all combined methods were being used at the same time.

Q. Were any benefits noticeable in those cases? A. From the Ensol?

Q. Just benefits generally.

I realize that you do not care to attribute the benefits to Ensol if the patient was undergoing one of the other recognized forms of treatment.

Did you notice any benefits, regardless of the reason for the benefit? A. Oh, yes: If the cause is removed by surgery you get benefit to the patient.

Q. Did you notice any benefit when the patient was being treated by x-ray or radium, regardless of the reason for the benefit? A. Yes, I have.

Q. Have you treated patients with Ensol when they were beyond x-ray, radium or surgical treatment? A. Yes; that is the greatest group, I think.

Q. Were those patients benefited by this treatment? A. I have no hesitancy in saying they were definitely so.

Mr. Connolly: The direct examination is closed.

Cross-Examination

By Mr. Mackey:

Q. I think you testified that in twelve cases there
134 was a reduction in pain.

Now, what does that reduction include, the reduction in pain include?

Does that include all the way from slight cessation in pain to complete disappearance? A. I would say "yes."

Q. How many cases of that twelve were there where you would say there was complete disappearance of pain? A.

Complete disappearance of pain? In approximately four.

Q. And I think you said in some of the cases you had treated both with Ensol and some of the other recognized forms of treatment. A. Yes.

Q. About how many would you say had combined treatment? A. There is only possibly three or four of the series that would be getting Ensol while they were getting their x-ray and radium. The others may have had previous surgery and they would get their Ensol after the other matters had been exhausted.

Q. Now, these four cases that had complete disappearance of pain, were they having any other treatment besides Ensol? A. No.

Mr. Mackey: That is all, thank you.

Mr. Connolly: I have no redirect examination.

* * * * *

C. Excerpts from Appellant's Documentary Exhibits.

1. Excerpts from Appellant's Exhibit 2 (Hendry Connell Research Foundation Bulletin No. 1).

(a.) Case histories.

251

Case 1

Mr. S.L., aged 49 years. Epidermoid carcinoma, proved by biopsy, originating in the left posterior nasopharynx and spreading to the frontal sinus, ethmoids, left antrum, anterior clinoid process and the frontal bone. Metastases had occurred in the cervical glands, but these had been treated with radium and surgery. The primary lesion had disappeared following deep radiation, but had recurred. The condition was of 1½ years' duration. While under observation this patient had been treated for syphilis, also for duodenal ulcer, requiring a gastro-enterostomy in 1934.

The case was referred as hopeless on May 10th, 1935. The patient complained of intense pain on the left side of the face and temple; marked bulging of the left eye; ptosis

and loss of vision in the left eye (p. 1. only); deafness in the left ear; marked cachexia.

Treatment with "ensol" was commenced on May 10, 1935. The dose was empirically set at 2 c.c., which at first caused some general malaise. After ten days' treatment the bulging eyelid showed some skin wrinkles. Vision was 20/100. Hearing in the ear had improved from C. V. 2 ft. to C. V. 18 ft. The patient became slightly upset and treatment was discontinued for a week. It was recommenced on May 28th. By June 7th the single daily dose had been increased to 4.5 c.c. He again became upset. When this upset cleared the dosage was changed to 0.5 - 1 c.c., alternating daily. On July 8th he had a typical bilious attack and treatment was discontinued entirely.

252 On September 7th the proptosis had completely disappeared. Except for a paralysis of the left levator palpebri, the left eye was as normal as the right. The pain had eased completely.

Case 2

Mrs. E.M., aged 45 years. The left ovary was removed on August 7, 1934, and found to contain papillomatous cysts which had involved the peritoneum. She was treated extensively with deep radiation following the operation.

On February 14, 1935, she was admitted to hospital complaining of severe crampy pelvic pain, constipation, bladder irritation, general cachexia and loss of weight.

Exploratory operation showed that the pelvis was matted with growth which had bound down the lower small intestine. Section of the growth was reported on as "secondary columnar cell carcinoma".

After discharge she was sent home to die. Morphia, to grs. iv daily, was required to ease the pain. The bowels were very constipated and required enemata.

Treatment with ensol was commenced May 14th as an experiment. An empirical dose of 2 c.c. was given every third day.

The patient steadily gained in weight, the bowels become normal, the appetite good. Opiates were reduced to heroin, gr. 1/12, which has since been discontinued entirely.

On September 7th the patient appears a normal healthy individual. She is doing her own housework, going on picnics and swimming. No opiates are used; weight gain, 32 lbs. since May. The bowels are normal, no laxatives being necessary.

* * * * *

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Case 6

Mrs. C.C., aged 70 years. Mixed cell sarcoma, proved by biopsy, over the right scapula extending into the axilla, with a second mass along the 9th, 10th, and 11th ribs in the posterior axillary fold.

The growth began in 1931. Extensive surgery, radium, and x-ray therapy have been used without lasting effect.

Referred on July 14th, when a biopsy was done for tissue to be used for producing autogenous ensol.

The main mass was fungating and was fixed tightly to the scapula. The second mass was ill defined, subcutaneous and hard as a rib. Pain was continuous over the mass, in the axilla and in the forearm. The patient was using opiates freely.

Treatment with ensol was commenced on July 15th. After ten days it was possible to ease the pain in all but the forearm. On July 29th the skin around the growth was irritated by a disinfecting solution and for a week no change in the pain was noticed. From August 5th to date the pain has been completely controlled. This is the first time since February, 1935, that *the patient has been completely free from pain*. She is taking no opiates at all.

Both growths show a marked change. The upper mass is puffy at the edges and can be moved slightly over the scapula. The lower mass has centred into a well-defined lump which is quite doughy. It also can be moved over the rib.

* * * * *

Mrs. L.W., aged 51 years. Carcinoma of the rectum; colostomy performed in 1931. She was fairly well until March, 1935, when a series of haemorrhages occurred. Since then she has been going gradually down hill.

Treatment with ensol was commenced on July 22nd. After five weeks' treatment her general condition has definitely improved and *the rectal pain has eased*.

* * * * *

Case 14

Miss G.B., aged 56 years. Secondary metastases from an original scirrhus growth in the right breast, in the head of the 8th rib and in the body of the 7th dorsal vertebra. The spine was markedly angulated and she complained of constant pain, but there was no paralysis.

Treatment with ensol was commenced on July 28th. The pain was controlled by August 7th. On August 29th the patient went home for a rest. *The pain has not returned to date*.

Case 15

Mr. F.C., aged 63 years. A mass in the bowel at the pelvi-rectal junction, adherent to the right side of the sacrum. Main complaints, pain over the sacrum and small thready stools. Cachexia is marked.

The case was diagnosed on July 25, 1935, and treatment with ensol commenced on July 27th. The treatment continued to September 4th. *The pain over the sacrum has lessened*. The stools are larger and his colour is good. Appetite is fair and the weight has remained stationary.

* * * * *

Mr. J.B., aged 76 years. Clinical evidence of carcinoma of the stomach. X-ray examination showed a filling defect at the pylorus and 75 per cent retention of barium. He complained of constant dull pain in the epigastrium, vomiting, anorexia and increasing weakness.

Treatment with ensol was commenced on July 29th.

On September 7th he was moderately improved. No vomiting; *the pain had subsided*; his appetite was fair, but the weakness had not improved.

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Case 24

Mrs. C.S., aged 46 years. Carcinoma of the cervix with extension to the bladder and rectum. Her main complaints were pain associated with the bladder and pain in the back and hips.

Treatment with ensol was commenced on July 28th. By September 1st the pain in the back and hips had been relieved, but the bladder pain was unchanged.

* * * * *

Case 27

Mrs. G.B., aged 40 years. Secondary metastases in both lungs from an original scirrhus carcinoma of the right breast. In June she had a collapse of the right lung and since that date complained of cough, chest pain, dyspnoea and weakness.

Treatment with ensol was commenced on July 31-st. By August 7th the breathing had improved slightly. By September 1st she was able to take moderate exercise without dyspnoea. *The pain in the chest was gone* and her general condition was moderately improved.

* * * * *

*Post mortem performed on the body of Mr. S. L. (Case 1)
at the Richardson Laboratory, 11th Nov., 1935*

Body: That of a poorly nourished Chinaman. Rigidity is present in the limbs. There is no lividity or post mortem change. There is a six-inch incision on the left side of the umbilicus in the abdomen. There is scarring on both sides of the neck, on the left side due to removal of glands and on the right side due to radium treatment.

Serous Sacs: Slight adhesions present on the left side of the chest. No adhesions on the right. Nothing to note in the pericardial and peritoneal sacs. There are adhesions between the liver and the diaphragm of a fibrous character and between the gall bladder and the caecum. There is an opening between the stomach on its greater curvature and upper part of the jejunum.

Heart: Shows some fibrous thickening of the mitral valve and to a less extent of the aortic valve. Cavities are filled with agonal clot on the right side. Muscle is pale and friable from toxic change.

Lungs: Left 300 gms. Right 475 gms. Both show emphysema of anterior borders and both show congestion and patchy consolidation of the posterior part of the lower lobes most marked on the right side.

Bronchi: Contain muco-pus and show congestion of their walls.

Aorta: Shows atheroma with calcification about the arch. Ascending portion beginning $1\frac{1}{2}$ " above the valve shows well marked leucic aortitis combined with atheromatous change.

Spleen: 180 gms. is enlarged and pale.

Liver: 1400 gms. Shows chronic periphepatitis. Surface rough from a degree of cirrhosis. Substance is tough and pale. Scattered through it are numerous secondary growths the largest is in the upper surface and measures 6 cms. across.

Gall Bladder: Is distended with thick bile. There are several enlarged glands infiltrated with growth between stomach and hilum of liver. Similar enlarged glands along ascending aorta.

Suprarenals: Appear to be normal.

281 **Stomach:** Shows opening into the small intestine on the greater curvature and just beyond the pylorus is a healed ulcer.

Kidneys: Left 150 gms. Right 140 gms. Both show pallor of cortex. Surface on stripping is smooth.

Head: On removing the calvarium the surface of the brain is oedematous and shows scattered areas of opacity. There are adhesions in the region of the left temporo-sphenoidal lobe and at this point a growth has burst through the bone of the skull. This growth is pressing on the lobe but not obviously infiltrating. Bone of the middle fossa is extensively softened from infiltration with the growth. A steel instrument can be passed into the pharynx and also into the antrum on the left side. Tissue of the left orbit is not obviously infiltrated. The optic nerve of the left side appears fibrous. Dura mater of the left side of the middle fossa shows numerous flattened masses of growth.

Summary: Carcinoma of pharynx with invasion of antrum and base of skull on the left side.

Large mass of growth within the cranial cavity pressing on the left temporo-sphenoidal lobe.

Masses of growth in dura mater.

Secondary deposits in liver and glands of abdomen.

Leutic aortitis in first part of aorta.

Atheroma of aorta.

Hypostatic pneumonia—bilateral, most marked on the right side.

Emphysema.

Fine cirrhosis of liver

Toxic changes in spleen and kidneys.

Death due to hypostatic pneumonia.

(Signed) JAMES MILLER,
Pathologist.

Comment by H. C. C.

It is evident that I was quite justified in the experimental use of a new biological product in this case. There was no harmful reaction, there was a recession of the orbital tumour and some mitigation of pain. There was a temporary return of vision. In any case it was impossible that he could live longer than a few weeks.

By means of this case I passed from laboratory work to clinical use.

Case 2.—Mrs. E. M., aged 45 years. This case was reported in the paper published in Oct. 1935. See reprint. It was stated that on Sept. 7th the patient appeared a normal healthy individual. She was doing her own housework, going to picnics and swimming. She had gained in weight 32 lbs. since May.

282 In October she began to show signs of bowel obstruction. On examination a hard mass could be palpated to the right of the mid line, directly beneath the incision scar. X-ray examination showed a partial obstruction at the recto-sigmoid junction.

On Oct. 23rd, an exploratory laparotomy was performed. The hard mass was found to be composed of dense adhesions binding the small and large bowel to the anterior wall. These were separated carefully and the right ovary was found in the centre. A section was taken for microscopic examination. See report. The pelvis was then examined. At the previous operation this was completely "frozen". At this operation the uterus could be palpated and there was a smooth outline to the whole pelvis although the rectum was drawn over to the right by adhesions.

After a slow convalescence, the patient complained of sciatic pain. X-ray examination showed no evidence of bone metastases. The pain was controlled for a time by novocain injections but the patient was very neurotic and rapidly built up a high morphine tolerance.

About March 9th, she began to show definite obstructive symptoms and later perforation was suspected. Knowing the condition of the abdomen further surgery was not attempted. Colostomy had been refused in October. The patient died March 14th.

Micro Examination, Tissue Removed Oct. 23rd

The material is almost entirely necrotic. Small areas show definite tumor acini, which are in parts regular in

their arrangement, showing the characters of a compound cystic adenoma. Other parts show appearances suggestive of malignancy with variation in shape and size of cell and a less clearly defined line of demarcation between acinus and stroma. Mitotic figures are not numerous and the whole appearance suggests a growth undergoing marked retrograde change.

Diagnosis,—Compound cystic ovarian adenoma largely necrotic, but with some areas suggestive of malignancy.

(Signed) JAMES MILLER,
Pathologist.

*Post Mortem performed on the body of Mrs. K. M. (Case 2),
at the Richardson Laboratory, 15th, March, 1936*

Body: That of a woman about 45 years of age. On the right segment of the lower abdomen are three healed surgical scars. The abdomen is distended and tense. Post mortem rigidity is not present.

The abdomen alone was examined. The cavity was opened to the left mid-line. The abdomen was full of coils of enormously distended large intestine. No tumour nodules were found in the abdomen. No peritonitis was present.

283 A large band of adhesions passes from the surgical scars above mentioned to the junction of the pelvic and sigmoid portions of the colon. Involved in this band is a tumour mass and a coil of small intestine.

The tumour mass consist of an ovarian tumour arising from the right ovary. It meaures about 25 cms. in diameter and is loculated in character, containing a few solid areas. The loculi contain brownish fluid. The mass lies in the hypogastrium about $\frac{2}{3}$ to the right and $\frac{1}{3}$ to the left of the mid-line. It is buried in a mass of adhesions connected with the band previously mentioned. The remainder of the pelvic contents are free from adhesions. No glands are found in Douglas pouch or along the aorta. In the mesentery of the small intestine were found two small glands but these show no infiltration.

The liver was smooth and showed a few adhesions in the neighbourhood of the gall bladder and above. Otherwise it showed no special features.

Summary: Cystic adenoma of right ovary.

Obstruction of the large bowel by band at the sigmoid-pelvic junction.

Partial obstruction of small intestine.

Perihepatitis.

(Signed) RONALD E. MURRAY,
Pathologist.

Post mortem performed under the supervision of Dr. W. T. Connell.

(Signed) W. T. CONNELL.

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(b.) Summary

1. Ensol contains an active principle which possesses the power to benefit proven cases of cancer by amelioration of symptoms and by partial or total disappearance of the growth.

2. The use of ensol is free from any unpleasant reaction to the patient—local or constitutional—nor does it harm them in any way.

3. This series is too small and the period of time too short to draw any definite conclusion as to the ultimate value of ensol, but it may be reasonably accepted that it does influence the course by partial or complete arrest in cases of advanced cancer.

4. The series is sufficiently large and the clinical improvement sufficiently constant to prove that the beneficial effect and regression in the growth observed, was not due to mere coincidence.

5. Ensol therapy was employed without any other therapeutic agent. When radium or deep irradiation had been used treatment was not commenced until the radiologist admitted that no further improvement could be expected from his form of therapy. In many cases he stated that further

irradiation would only aggravate the disease and cause increased pain.

6. Case 11 (scirrhus carcinoma of the breast) which had no other treatment, improved after one month's ensol therapy to such a degree that the growth diminished by 75% with corresponding clinical improvement.

As in syphilis and other constitutional diseases one course of ensol therapy will not suffice but repeated courses will be necessary for the continuance of the beneficial influence of ensol on cancer.

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411

2. Summary of Recent Cases

G. S. Burton, M.D.

From Appellant's Exhibit 3.

From May 1st to Oct. 30th, 1936, many cases applying for treatment were rejected by correspondence as they were obviously in the very late stages of the disease.

One hundred and fifty cases were admitted to the clinic and of these fifty-six were not treated. Three were found to be not malignant; in six treatment was postponed and two were sent home with ensol to be used by the attending physician. The remaining forty-five were so hopeless and far advanced they were advised to return home.

Of the ninety-four cases treated eighty-three were also advanced and all had received all the benefit possible from surgery, X-ray and radium. They had been told that nothing more could be done for them. Of these eighty-three, twenty did not respond to treatment or appear to be changed or benefitted by it during the period they were under observation. Sixty-three responded to a greater or less degree, varying from mitigation of severity of symptoms to definite progress towards recovery of good health.

These figures indicate that ensol treatment is still being utilized almost entirely among those abandoned to die in the very near future. For research purposes it is an excellent field of work and it is a great satisfaction that so much has been done for them. Some observers have advanced

the statement that a remedy such as ensol should "cure" all cases. We are not so optimistic. When tissue has been destroyed and function seriously impaired there is no possibility of recovery.

557

3. Pain in Malignant Disease

J. C. Connell, M.A., M.D., C.M., LL.D.

From Appellant's Exhibit 4.

Three hundred and eighty-two cases of cancer were studied in relation to the symptom of pain. Of these 93 or 24% had no pain or it was of so slight a character that treatment for its alleviation was not necessary.

The other 289 cases required drugs in some form for relief of pain. All these received Ensol treatment and in 279 or 96%, pain was partially or completely relieved. While a much larger group should be studied to give accurate percentages it can be said that approximately 76% of cases of malignant disease require medication for the relief of pain. Further it appears that 73% of all cases of cancer treated with Ensol were relieved of pain in some degree.

In 93 cases pain was not a symptom. The reason for this is not understood. It is not anatomical or regional as the following figures show. The regional distribution of 93 cases was as follows:—

Breast	34
Rectum	11
Ovaries	10
Stomach	8
Larynx	5
Uterus	4
Colon	4
Oesophagus	3
Lung	
Neck	
Pelvi-rectal	2 each
Groin	
Liver	
Kidney	
Face	
Forehead	
Testicle	
Arm	
Pelvis	1 each

These cases were of all degrees of severity and with and without metastases. Evidently from these figures an anatomical or regional basis will not explain pain or its
558 absence. This distribution follows quite closely that of all cases examined at this clinic.

The common sense view of pain is that it is a reaction of the sensory nervous system to a prejudicial activity. It may be easier to decide why there is pain in a particular case than to learn why it is present in one case and not in another of apparently similar character. The obvious causes of pain are inflammation, pressure, stretching of muscle or nerve fibre and toxæmia.

Treatment of Cancer with Ensol a Preliminary Report
By Neville Davis, M.B. Ch.M.

556

Summary.

1. Ensol has been used in Australia during the past 20 months to treat hopeless, incurable, and advanced cases of cancer, with encouraging results.

2. It has been shown to possess a specific action on cancer cells, both experimentally and clinically, producing destruction of the cells with disintegration of the nucleus.

3. Ensol treatment has produced necrosis of cancerous growths which have entirely disappeared. This has occurred in nearly 25 per cent. of cases treated.

4. No claim is made that Ensol is a cure for cancer. There has been insufficient time for the consideration of this phase.

5. Ensol injections do not cause patients any serious discomfort. On the contrary, even in extreme cases with ultimate death of the patient, it has been shown to give relief of pain, diminish the quantity of opiates used, improve appetite, increase weight, generally relieving distressing symptoms.

6. Ensol has been shown to restore to normal, the biochemical constituents of the blood that are subject to variation in cancer patients.

7. Ensol has been used in a prophylactic manner, but no attempt is made to draw conclusions as to its efficacy in this report.

8. It is recommended that Ensol should be used in all cases of cancer at all stages of the disease. It can be used in conjunction with other accepted forms of treatment (surgery, radium and X-radiation).

9. Ensol has been used to treat melanoma and sarcoma. The results are promising.

References:

1. Bio-chemical Studies on Cancer Patients Treated with Ensol, Munro, F. L., *Bulletin*, Hendry-Connell Research Foundation, I:76 (1936).

2. Personal communications.

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4. Rectal Carcinoma**How Best Handled**

Thos. F. McNamara, M.D.,
Rochester, N. Y.

Appellant's Exhibit 6.

(Reprint from The Journal of The American College of Proctology, December, 1938).

When I saw by the Journal that Dr. Davis had assigned this subject to me I was pleased because I thought it would not take much of your time to tell what I know about it. In thinking it over, however, I came to the conclusion that to decide what is best to do for a patient by the time he comes to the doctor is one of the most difficult tasks with which the physician and surgeon has to deal.

The great majority of patients that have consulted me gave a history of having had for about two years what he or she thought to be a case of hemorrhoids. The usual remark is "Doctor, I have been putting off coming to see you for about two years, but my hemorrhoids are now giving me so much trouble and pain that I cannot stand it any longer."

While taking a history of the case, getting a line on the symptoms, and noting the general appearance of the patient, we invariably come to the conclusion that the condition is something much more serious than hemorrhoids. We make a digital examination and one of the first things we encounter is an abnormal mass. In the great majority of cases, if it is cancer, we find it in the rectosigmoidal junction.

574 In a small percentage of cases we find the growth in the rectal ampulla. In a small percentage of cases the patient will usually give a history of having had trouble anywhere from a period of five to ten months. Being situated in a more sensitive area, the symptoms of pain, a feeling of fullness in the rectum that is not relieved by an evacuation, etc., show up much earlier than when the tumor is at the junction of the rectum and sigmoid. In the latter condi-

tion the patient is not so much emaciated as in the other variety. Has not lost weight to any great extent.

Most of the cases I have seen with the growth at the recto-sigmoidal junction, the growth had advanced to such an extent that a radical operation such as resection of the rectum following colostomy could not be performed with any hope of cure, nor without great danger to the patient. In two such cases where the physical condition of the patients was such as to justify taking a chance, the patients died of uremia about a week after the operation. One of the patients was 65 years old, and the other past 70. Each seemed to be in splendid physical condition, although the former was rather a fleshy man. Fleshy people are always poor risks, and more especially when the patient is a man.

The operation is not so difficult with women as with men on account of the greater pelvic space, and the lesser difficulty in separating the rectum from the surrounding organs. The surgeons who operated these cases are among the best in the country.

Most cases of cancer of the rectum occur in elderly people.

The greater the age, other things being equal, the
575 greater the risk. As a rule I would say that any patient beyond the age of 65 is a poor risk. However there may be an occasional exception to this rule, and, if so, I would leave it to the judgment of the surgeon.

As to the condition of the growth, if it is adherent to surrounding organs, has penetrated beyond the muscular coat, is not movable on palpation, or there is much glandular involvement, it is not a case for the radical operation. Glandular involvement however may not always mean extension of the growth, as it is sometimes due to inflammation or sepsis.

If the growth is so high that the finger cannot reach above the upper edge of the growth, it is not a case for a complete operation by the perineal route. A case that requires going into the pelvis from above is always more dangerous, as it is always more difficult—great danger of shock. In the small percentage of cases where the growth is in the rectal am-

pulla and the anus, diagnosis is sometimes made early enough so the chance of successful operation is better than in another locality.

If, however, the inguinal glands are affected, it cannot be cured by operation. Some authorities say that a cancer at the annus is best treated by radium. Occasionally a growth in the rectal ampulla may be removed without taking out the rectum. Such is true when it is movable and has not penetrated below the muscular coat. We cannot always judge by the size of the growth, as a small one may be found to have spread more than one that is larger on the surface.

Now, what should be done with cases that are inoperable, as are most of them when they come to us? For
 576 many years I referred cases to the New York State Institution for the Study and Treatment of Malignant Diseases. None of the patients survived more than two years. They were treated by radium and x-ray. One died under an anæsthetic, while radium seeds were being planted, the first day he was at the clinic. A woman who had been doing her housework up to two weeks before going to the institution, died ten days after returning home. She had been taking x-ray treatments for two weeks. The cause of death as I saw it was lymphatic infection all around the rectum. In other cases, the radium caused sloughing of the growth, so that obstruction did not occur as early as it might have otherwise. In none of the cases was a colostomy done. If it had been done, and the growth not removed, the effect would have been to prolong a life of misery and suffering.

At the Lahey Clinic in Boston x-ray treatments are never given for cancer of the rectum. The claim is that at the time the patient comes to the doctor, the tissue is more or less broken down and infected, and that infected tissue in that location will not respond to x-ray. I do not know whether they depend on radium in any cases.

In the operated cases at the clinic statistics show that 42 per cent are alive and well five years or more after the radical operation, following colostomy. This is a good record, as many of the people are well along in years, but the

percentage of cures depends on the judgment used in selecting the cases, as well as the skill of the surgeon.

The extreme prostration and weakness caused by x-ray treatments, would be justified if they cured, but I doubt if they ever do.

577 Should colostomy be done in hopeless cases? If I were to be the patient I would say "No". The best it can do is to prolong for a few months or perhaps a year of life of suffering.

I knew a physician aged 60 who had a colostomy and was able to work for a short time thereafter. I don't think I ever knew a patient to suffer with anything, as he did before he was relieved by death. The sloughing of tissue from surrounding organs was terrible. While still at work, he said to me one day, "I work all day and suffer pain at night." I said if I were you I would take a fourth of morphine at night. He did not take kindly to the suggestion, and asked, "Do you want me to become a drug addict?" *For a long time before he died he was taking three grains of morphine every three hours, and then did not get relief. Up to that time I did not know that a person could take 24 grains of morphine in as many hours.*

If the time ever comes that people will consult a physician at the first indication of rectal trouble, as they do with eye, nose and throat troubles, the death rate from cancer will decrease, instead of increasing as shown by statistics at the present time and for many years back.

From April 1937 to April 1938 there were seven cases of cancer of the rectum among my cases. Two of those had a colostomy and excision of the rectum early last spring. At this date they seem to be doing fairly well. One of them is taking x-ray treatments. Two are dead. Two are confined to their beds in a hopeless condition. *The one patient of mine that is still on his feet, and working every day, is one that has had no operation of any kind, and no radium or x-ray treatments.*

578 We have cancer committees all over the country, and physicians and laity are thoroughly aroused in an

effort to curb the monster. We have heard many talks over the radio, asking people to be on the alert, and to watch out for any growths on the surface of the body, but I have never yet heard one speak of cancer of the rectum. Would we be justified in scaring 97 per cent of people with rectal troubles by such talks, in an effort to gather in 3 per cent that would have symptoms of malignancy?

I always ask my patients to send in their afflicted friends no matter how slight their troubles may be. The management of cases of malignancy that are far advanced, does not mean much. The great question is how to reach the cases that we could benefit provided we could reach them in time.

The early symptoms of carcinoma at the recto-sigmoidal junction are inability to empty the bowels satisfactorily followed by periods of diarrhoea often coming on early in the morning, retention and pressure by gas. Will get relief after taking a cathartic, and perhaps feel well for a couple of days, only to have a repetition of the symptoms. Discharge of mucous and finally mucous mixed with blood. Lastly, pain.

Now, I would like to take the time to read to you a few results from the use of Ensol, which is what I used for my patient who is still on his feet. There are a number of cases cited in this book but I shall read of just two.

“Biopsy proof. Symptoms present two years before positive diagnosis made. Colostomy May, 1936. Admitted June 30, 1936. Pain in lower sacral region, discharge 579 and bleeding from the rectum. Weight 146 pounds.

Ensol was used from July, 1936, to date. There has been a marked general improvement, a twenty-two pound gain in weight maintained to the present time. There is no bleeding and the discharge has been very definitely diminished. *The pain symptom has been relieved and the patient has not been receiving any type of analgesic.”*

“Biopsy proof. Rectal hemorrhage in April, 1936, diagnosis was made. Surgery was refused. Admitted September, 1936. There was rectal bleeding, fatigue on exertion, pain in the right hip. Examination showed a transverse

growth, fixed about two and one-half inches from the anus. Did not report for treatment until January 1, 1937, and since that time treatment with Ensol has been continuous. The weight has been maintained, the symptoms have been relieved, the rectal ulceration has regressed."

I wrote and told the Hendry Connell Research Foundation I was going to read a paper to this society and asked them for any literature for distribution and told them I would be as conservative as possible in presenting this to you. They make no claims whatever for cures. It can be used in conjunction with anything else that you are doing. Report from Dr. McNamara, dated December 27th, 1938, of case to which reference is made in above reprint.

"In March, 1938, Mr. G.— came to the office with a history of having suffered with rectal trouble for upwards of seven months.

For some time he had suffered pain, and there was sloughing, with considerable clotted blood in the stools.

580 Biopsy confirmed the diagnosis of adeno-carcinoma, and was said to be of a fast-growing variety.

The patient was 42 years of age and had been working up to the time he consulted us. On May 31st, 1938, the first treatment of Ensol was given. He was able to continue with his work, and at present is putting in full time. *The pain, sloughing, bleeding, discontinued about two months after the treatment had begun.*

The patient has maintained his usual weight, has a good appetite, looks well and he claims he is feeling better than he had felt in a long time. The growth, at first rough and irregular, is now smooth, and as far as I can determine by digital examination is somewhat reduced in size. He has had no operation, no X-ray or radium treatments."

5. *Ensol as an Aid in the Treatment of Rectal Cancer.*

581

Appellant's Exhibit 7

GLENN S. BURTON, M.D., C.M.,
Kingston, Ontario

Hendry-Connell Research Foundation

(Reprint from The Journal of The American College of
Proctology, March, 1939.)

Ensol is a biologic solution which has a palliating influence in the treatment of cancer. The clinical use of Ensol has progressed since May, 1935, to a point where many physicians, surgeons, and radiologists in Canada and the United States are adding it to other resources in the management of the cancer patient.

From the statistical evidence available as to end results in rectal cancer, more is needed to control the disease than early diagnosis and local treatment.

We have demonstrated that antigens may be extracted from cancer tissue by bacterial digestion. These antigens as contained in Ensol are active and will stimulate the production in antibodies in the cancer patient. This biologic approach to cancer control suggests the possibility of an effective attack on a constitutional disorder.

For your consideration ninety cases of rectal cancer treated at our clinic are reviewed.

Males, 67; Females, 23.

Ages: 37-80, the largest group in their late fifties.

Adenocarcinoma was the type in practically all the cases of which 57 were of the fungating type and 32 annular in character.

582 Known duration of the disease varied from two cases of five years to 14 cases of only six month duration.

Fifty-one cases reported symptoms to have been present over one year. It is interesting to observe that of the four-

teen cases of six months duration there were three with advanced liver metastases.

One-third of the cases had had surgery; one-fourth of the cases had had radiation before their admission to our clinic.

It should be stated at this point that it has always been our policy in the management of our cases that where surgery and/or radiation was indicated, advice to this effect was given the patient.

Of the 90 cases admitted, 9 were not treated as obstruction or a terminal condition was present. Twenty-two cases of advanced cancer received less than 30 cc. of Ensol and have been deducted from the total number on the grounds of inadequate treatment.

Of the 59 cases of rectal cancer treated with Ensol over a period varying from two months to three and a half years there were 43 cases, or approximately 75 per cent who received benefit as estimated by pain relief and symptomatic improvement. Sixteen cases were not benefited. It is to be remembered that all these cases had already received all that could be done for them by accepted methods of treatment.

Realizing that case histories are always interesting to the practicing physician, twenty are submitted for your attention. The first ten cases are taken from our own admissions, the other group are cases treated by independent physicians with Ensol supplied from our Foundation.

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591 6. *Relief of Pain in Cancer by the Use of Ensol.**Appellant's Exhibit 8*

Submitted to the Ontario Commission for the Investigation
of Cancer Remedies

by the

Hendry-Connell Research Foundation

Kingston, Ont., May, 1940.

About 75% of cases of malignant disease require medication for the relief of pain. Morphia and its derivatives are commonly used for the purpose.

Clinical experience during the past five years has shown that about 90% of these cases with pain, can be partially or completely relieved by the use of Ensol. No explanation is advanced for this pain relief. As progress is made in the investigation the reason for pain relief may become apparent.

The following extracts from clinical histories and progress reports of cases under treatment with Ensol, illustrate the results observed.

Case 2. - - F. Carcinoma, extensive involvement of entire pelvis. Ensol given May 15/35. *Marked relief of pain* and narcotics discontinued. Returned to good health and lived for ten months when death was due to intestinal obstruction from surgical adhesions.

Case 7. - - F. Carcinoma cervix uteri. Ensol given over a period of four months was accompanied by *definite pain control*.

Case 13. - - F. Carcinoma, both breasts; advanced case. Had intermittent treatment with Ensol for over a year with temporary improvement and *relief from pain*.

Case 21. - - M. Carcinoma, prostate with secondaries. Uraemic when admitted. Had marked improvement with *relief from pain*. Lived six months.

Case 24. - - F. Carcinoma, uterus. Under treatment for three months. *Pain relief* the only benefit noticed.

Case 26. - - F. Carcinoma, breast with secondaries in sacrum, hip, right shoulder, humerus, scapula and clavicle. Far advanced case. Following the use of Ensol there was general improvement, *freedom from pain* and comfortable existence for a year and nine months.

Case 27. - - F. Carcinoma, breast with extension to chest. Recurrence one year after operation. Pronounced hopeless case before Ensol was used. Treated intermittently from July/35 with return to good health. *Pain in chest disappeared entirely*. Died three years and four months after the first use of Ensol. Cause of death pneumonia.

Case 29. - - F. Carcinoma, cervix. Advanced case. Lived for over a year after the first use of Ensol with gradual advance of the lesion but *pain was controlled*.

Case 30. - - M. Carcinoma, pelvic colon. Treated from July/35 to April/38,—two years and nine months, during which time he made temporary improvement, gained in weight and was *free from pain*.

Case 31. - - F. Carcinoma, breast with secondaries in chest. Treated from July/35 to Jan./37. Marked improvement. Had been bedridden but recovered to get about and live comfortably for one year and five months. *Pain disappeared*. Died of pneumonia.

Case 35. - - F. Sarcoma, right humerus. Under
593 treatment with Ensol *pain was controlled*. When Ensol discontinued pain returned. Lived four months.

Case 47. - - F. Carcinoma, breast with secondaries in chest, skull and abdomen. Under treatment from Aug./35 to June/36 with marked improvement for the first six months. *Pain was controlled* till time of death in June/36.

Case 51. - - M. Carcinoma, rectum. Advanced case. Under treatment Aug./35 to Oct./36,—one year and two months. Made partial recovery and *became quite free from pain*.

Case 53. - - M. Carcinoma, colon and prostate. Three months under treatment. *Pain diminished* but not completely controlled.

Case 58. - - F. Carcinoma, breast with secondaries in hip and chest. Treated from Aug./35 to June/36,—ten months. Had spontaneous fracture of femur in April but was kept *free from pain*.

Case 59. - - F. Carcinoma, breast, spine, femur. This was near termination but Ensol gave *great relief from pain* during the two months which remained of life.

Case 59-B. - - F. Carcinoma, rectum. Treated from Aug./35 to Feb./37, one year and six months. Improvement was marked for over a year, then progressed to the end but was *almost entirely free from pain*.

Case 61. - - M. Carcinoma, colon. Improved under Ensol, became *free from pain* and returned to work. No further report on this case after seven months when he was still at work.

Case 65. - - M. Carcinoma, right shoulder. Treated from Aug./35 to Sept./36 with general improvement but gradual extension of the ulcerated area. Under Ensol was *kept free from pain*.

594 Case 70. - - F. Carcinoma, uterus. Under treatment from Aug./35 with great improvement and *relief of pain*. Six months later died of pneumonia.

Case 73. - - M. Carcinoma, left jaw. Far advanced when taken on treatment Aug./35. Continued to be progressive but *pain relief was marked*. Lived one year and eight months after beginning treatment.

Case 82. - - F. Carcinoma, rectum. Treated from Aug./35 intermittently to date April/40,—four years and four months. Gradually improved with *complete relief of pain*. Recovered good health and remains well, living a normal life.

Case 89. - - F. Carcinoma, breast with secondaries in spine. Improved to a considerable degree. Axillary glands disappeared. Lived two years and eight months in comparative comfort and was *almost free from pain*.

Case 90. - - M. Carcinoma, kidney. Lived eleven months. Ensol made him more comfortable and *kept him free from pain*.

Case 95. - - M. Carcinoma, prostate. Treated from Aug./35 to Oct./36. *Relief of pain was complete*, gained in weight and remained fairly well. Had one year and two months of relative comfort under Ensol.

Case 96. - - F. Carcinoma, breast with involvement of axillary glands. Improved rapidly and became *free from pain*. Treatment began Aug. 14/35 and has continued to date, April, 1940,—four years and eight months. Patient is living a normal life.

Case N. D. 3. - - M. Carcinoma, colon with meta-
595 stasis in liver. After eight weeks treatment with Ensol showed marked improvement, *pain diminished*, weight increased 14 lbs., liver regressed in size, return of appetite.

Case 101. - - F. Carcinoma, breast. Treated from August/35. There was general improvement, *relief of pain* and return to fairly good health. Last report June/37 was very well.

Case 102. - - F. Carcinoma, breast. Treated over a period of eight months when death occurred. There was temporary general improvement and *pain was controlled*.

Case 103. - - M. Carcinoma, tongue with secondaries in cervical glands. Treated with Ensol over a period of three months during which there was some general improvement and *local pain relief*. Died suddenly.

Case 105. - - F. Carcinoma, both breasts, Treated with Ensol over a period of seven months with *relief of pain*, some healing of ulcerated surfaces and general improvement.

Case 113. - - F. Carcinoma, breast. *Pain in arm began to disappear after the third injection of Ensol*. At the same time there was softening of the enlarged glands in the axilla and supraclavicular areas. The patient was still living one year and four months after the first use of Ensol.

Case 115. - - F. Carcinoma, breast with metastases in spine and pelvis. Pain was severe but gradually subsided under treatment with Ensol. In two months was *entirely*

free from pain and did not require narcotics. Lived eight months with very little pain up to termination.

Case 117. - - M. Carcinoma, stomach. History 596 of six months before the use of Ensol. *Pain was severe. Was brought under control* and remained comfortable till the end three months later.

Case 118. - - F. Carcinoma, breast with secondaries in bones of pelvis. After two months under Ensol was able to walk again *without pain*. Temporary improvement continued for six months. Lived eight months after the first use of Ensol.

Case 119. - - M. Carcinoma, oesophagus. Dysphagia severe. History of three months. After a week of treatment with Ensol swallowing became better. Was eating light solids and *pain was controlled*. Weight increased. At the end of three months went home for a rest, developed a septic throat and died.

Case 120. - - F. Carcinoma, upper lip and hard palate. History of six months before the use of Ensol. After a week swelling became less, discharge ceased and *pain was relieved*. Lived for six months without much pain.

Case 124. - - M. Carcinoma, stomach. After a month of treatment with Ensol, was eating well, *pain had diminished* and weight had increased by 7 lbs. General condition maintained. Lived for ten months.

Case 129. - - M. Carcinoma, bladder and prostate. Advanced case. Lived five months after the first use of Ensol. *Pain was controlled* and there was temporary general improvement.

Case 130. - - F. Carcinoma, breast. Gained seven pounds in weight during the first three weeks after the use of Ensol. *Pain was controlled* and general condition improved. Lived seven months after treatment began.

Case 133. - - M. Carcinoma, colon. During the 597 first month of treatment with Ensol weight increased 6 lbs. and bowels became regular. *Pain ceased*. After six months died of acute obstruction of the bowels.

Case 137. - - F. Carcinoma, Colon. Advanced case. After ten days treatment with Ensol was *free from pain*. Lived four months in comparative comfort.

Case 138. - - F. Carcinoma, ovaries. Began treatment in August/35. Improved gradually and *became free from pain*. Returned to normal health and usual manner of living. Remains well to date, April, 1940,—four years and eight months after the first treatment. Had no other treatment except Ensol.

Case 139. - - F. Carcinoma, bladder with metastases in abdomen. Under Ensol became much more comfortable and *free from pain*. Lived for three months.

Case 144. - - F. Carcinoma, breast. Following use of Ensol, incision and ulceration healed, some keloid, no glands palpable in axilla or supraclavicular area. *No pain*. Treatment discontinued after four months. Two years and three months later no evidence of recurrence. In good health.

Case 150. - - F. Carcinoma, mouth, chin and face. After two weeks treatment large mass sloughed out. *Free from pain*. Treatment continued. Lived five months.

Case 153. - - F. Carcinoma, head of pancreas. During the first month of treatment with Ensol gained 3½ lbs. in weight, improved generally and became *free from pain*. Lived in fairly comfortable state until Jan./37 when she died, one year and six months after first treatment.

Case 156. - - M. Carcinoma, liver and abdomen.
598 Pain severe. After three days treatment with Ensol *pain was less and gradually disappeared*. Lived for three months. Died following a solostomy for intestinal obstruction.

Case 160. - - F. Carcinoma, oesophagus. Dysphagia advanced. After two weeks treatment was swallowing better, no nausea or pain. Temporary improvement. Lived four months.

Case 166. - - M. Carcinoma, rectum. Advanced case. *Pain was relieved* and there was some general improvement for several months. Lived four months.

Case 169. - - F. Carcinoma, breast with secondaries, bones of pelvis. Pain severe, bedridden. After three weeks of Ensol was able to sit up and later to walk about. Developed migrane, probably metastasis to skull. *Pain relief was temporary.* Died after five months.

Case 171. - - F. Carcinoma, breast with gall bladder involvement. After two months treatment *pain was less*, swelling reduced and general improvement. Lived seven months.

Case 175. - - M. Carcinoma, rectum. There was marked general improvement with *relief from pain.* Lived two years and seven months after the first use of Ensol.

Case 195. - - M. Carcinoma, colon. Growth was greatly reduced after a month of treatment with Ensol and *pain was relieved.* In four months weight increased by 17 lbs., abdomen reduced 4". Temporary improvement in this case was marked. Lived six months.

Case 200. - - F. Carcinoma, breast and metastases to chest. Fluid in lung, dyspnoea, pain in arm. In less than a month after treatment with Ensol was *free of pain*,
599 breathing easier and became generally improved.

Lived for one year and four months fairly comfortable.

Case 203. - - F. Carcinoma, colon. Severe pain. After a week on treatment with Ensol *pain was less* and soon was under control. At the end of two months an abdominal abscess was opened and drained. Further improvement, *no pain and little tenderness.* Died at the end of six months.

Case 207. - - F. Sarcoma, right forearm. *Pain in the arm ceased* after two weeks under Ensol. At the end of three months the arm was less swollen. Nine months after initial treatment was carrying on. No later report.

Case 209. - - M. Carcinoma, breast. Pain was severe. At the end of two weeks *pain much less.* In a month pain under complete control.

Case 211. - - F. Carcinoma, breast. Pain was severe in the line of incision of old operation. After the fourth dose

of Ensol *pain* ceased. Lived comfortably for nine months.

Case 221. - - M. Carcinoma, bladder. Constant pain and irritation. Rapid improvement with *cessation of pain*. In two months gained 17 lbs. in weight. Lived comfortably and died suddenly at the end of six months.

Case 230. - - F. Carcinoma, breast with involvement of the chest, Dyspnoea. There was temporary improvement with *relief of pain* for several months. Weight increased. Then relapse with increasing dyspnoea. Liven seven months.

Case 232. - - F. Carcinoma, ovary. After four months of treatment with Ensol *pain had disappeared* as also the mass in the left lower abdomen. General condition greatly improved.

600 Case 240. - - F. Carcinoma, vulva. Under Ensol treatment, improved rapidly in general condition, with gain in weight and *freedom from pain*. There was recurrence in inguinal glands. These were excised with return to good health. Treatment began Sept./35 and continued with some regularity to the present, April/40. Patient now in good health.

Case 255. - - M. Carcinoma, face. Pain severe. *Pain brought under control in about two weeks*. Between Oct. 1/35 and Jan. 18/36 gained 28 lbs. in weight and returned to good health. Continued well for two years and three months. Then relapse but Ensol treatment not resumed.

Case 267. - - F. Carcinoma, vulva. Pain in lesion, in neck, arm and side. This was *gradually relieved*. Lived for nine months with a fair degree of comfort.

Case 268. - - M. Carcinoma, prostate. Pain was severe. After ten days treatment *pain was under control*, narcotics were discontinued. Lived one year and two months after beginning Ensol.

Case 269. - - F. Lympho-sarcoma, neck. Treatment with Ensol began in Oct./35. After two months the glands in the neck were greatly reduced and *pain disappeared*. Gen-

eral condition was improved. Reported very well in Oct./37,—two years later. No further reports received.

Case 272. - - F. Carcinoma, ovary. Improved to a marked degree and became *free of pain*. Was transferred for treatment to Vancouver. Lived for two years and four months after the first use of Ensol.

Case 277. - - F. Carcinoma, larynx. Local and general condition much improved and became *pain free*.
601 Lived one year and five months after the use of Ensol.

Case 279. - - F. Carcinoma, stomach. Rapid improvement with *relief of pain*. Relapse took place after three months but remained free from pain. Lived six months.

Case 258. - - M. Carcinoma, pancreas. Pain in upper abdomen severe. Slowly improved, became *free from pain*. First treated in Oct./35. Returned to normal health and is still living, April, 1940.

Case 286. - - M. Carcinoma, stomach. Pain was constant and aggravated by food. After a month of treatment with Ensol *pain was controlled*, appetite improved and there was a good gain in weight. Lived two years.

Case 289. - - M. Carcinoma, lip with secondaries in the neck. There was immediate *relief from pain*, temporary general improvement with some regression of the glands in the neck. Lived five months.

Case 307. - - F. Carcinoma, breast (Paget's) with involvement of supraclavicular glands. During the first month of treatment the whole area which was hard and nodular became soft and doughy and the glands moveable and there was *no pain*. Temporary improvement. Lived nine months.

Case 314. - - F. Carcinoma, colon. This was a case near termination taken on for treatment for *palliation of pain*. This was secured and the patient lived for four months.

Case 318. - - M. Carcinoma, rectum. Ensol gave *immediate relief from pain*. An advanced case but lived for a year after the first use of Ensol.

Case 335. - - M. Carcinoma, right bronchus, dyspnoea with pain in chest. Within ten days *pain was relieved*, breathing became easier and there was a gradual return to good health. This patient had been abandoned at the Mayo clinic as a hopeless case before beginning the use of Ensol. He returned to work, is still living and working and in fairly good health. Treatment began in October, 1935, carried on more or less regularly to date. April, 1940,—four years and six months.

Case 384. - - M. Endothelioma, left cheek, nasal fossa and orbit. Severe pain. During the first month of treatment *pain ceased*, there was general improvement with better appetite. Lived for eight months in fair comfort.

Case 387. - - F. Carcinoma, rectum. Advanced case. *Pain was relieved*, narcotics discontinued. Temporary general improvement. Lived one year.

Case 408. - - M. Carcinoma, rectum with involvement of testicles. Under Ensol *pain was relieved*, swelling of testicles reduced and generally felt better. In two months increased 14 lbs. in weight. Lived for six months.

Case 412. - - F. Carcinoma, ovaries. An advanced case with cystitis. Pain was a marked symptom. Began treatment Dec./35. During January, 1936, *became pain free*, returned to fairly good health and resumed care of her own house. Lived comfortably for over three years.

Case 418. - - M. Carcinoma, rectum. Under Ensol between Nov. 7th and Dec. 13th general condition improved, *pain was relieved* and weight increased. Improvement maintained for about a year. Lived one year and four months after beginning Ensol.

Case 421. - - F. Carcinoma, rectum. Advanced case. Improved under Ensol, *free of pain*. At the end of 602a three months her condition was generally satisfactory. Treatment discontinued at the end of one year and nine months. No later report.

Case 432. - - M. Carcinoma, stomach. History of eight months before beginning Ensol. Appetite improved, felt

stronger, *pain disappeared* and became comfortable. Lived for one year and two months.

Case 434. - - M. Carcinoma, rectum. Between Nov. 12th and Feb. 1st gradually improved, *pain gradually became less* and then ceased. Lived two years and four months after the first use of Ensol.

Case 455. - - M. Carcinoma, colon, sigmoid. In two months under Ensol gained five pounds in weight, *was relieved* of pain and felt very well. Rectal growth became more moveable. Lived for over three years.

Case 456. - - F. Carcinoma, oesophagus. Between Nov. 25th and Dec. 22nd swallowing improved with *less pain*. Then gastrostomy was done and patient lived for one year and seven months in comparative comfort.

Case 462. - - F. Carcinoma, uterus. Advanced case. Between Nov. 28th and Dec. 20th uterus decreased two-thirds in size, *pain was relieved* and general improvement marked. On May 1st uterus was almost normal in size, no fixation, walls smoother. Recovered fairly good health and lived over two years after the first use of Ensol.

Case 464 - - F. Carcinoma, breast. Under treatment from Dec. 4th/35 to April 6th/36 marked improvement with *complete relief of pain*. Recovered normal health. Patient still living in good health four years and three months after the first use of Ensol.

603 Case 471. - - F. Carcinoma, cervix. Right breast removed in 1933. Left breast in 1934. Cervix lesion developed in 1935. Treatment with Ensol beginning in Nov./35. Rapid improvement with *relief of pain*. Two months later doctor reported, feeling well, gained eight pounds in weight and had returned to work.

Case 482. - - F. Carcinoma, breast. General condition improved, glands in neck regressed and *pain ceased*. Lived one year and five months after the first use of Ensol.

Case 502. - - M. Carcinoma, rectum. Treatment given for palliation of symptoms. After ten days treatment

pain was diminished. Lived four months and remained comparatively free from pain.

Case 503. - - M. Carcinoma, thumb with enlargement of glands in axilla. Pain severe in hand and arm. Treatment for a month with Ensol, local and general condition improved. *Pain less.* One year and a half later had completely recovered, thumb healed, nothing palpable in axilla.

Case 506. - - M. Carcinoma, rectum. Advanced case. Became stronger, was *free from pain* and gained in weight. Was able to resume golf and felt very well. This continued for several months, then relapse. Lived nine months.

Case 514. - - F. Carcinoma, thyroid and cervical glands. Softening of the mass and of the glands took place following the use of Ensol. *Pain was relieved.* Continued for several months and then relapsed. Lived six months.

Case 519. - - M. Carcinoma, rectum. Advanced case. Under Ensol mass became less fixed, *tenderness and pain were relieved*, bleeding ceased and there was partial return to good health. Lived one year and eleven months
604 after the first use of Ensol.

Case 521. - - F. Carcinoma, breast with involvement of supraclavicular glands and chest. There was local and general improvement with less swelling and *relief of pain.* Lived one year and four months.

Case 524. - - M. Carcinoma, rectum. Mass encircling rectum. Pain very severe. Under Ensol mass became softer, bleeding ceased and *pain was controlled.* In first two months gained eight and a half pounds. There was marked general improvement. Lived one year and six months.

Case 525. - - F. Carcinoma, breast with enlargement of axillary glands. Definite improvement with *relief of pain.* Lived two years and four months.

Case 526. - - F. Carcinoma, rectum. Greatly improved under treatment and lived for over four years after beginning treatment. *Pain was completely relieved.*

Case 530. - - F. Carcinoma, breast with involvement of deep supra-clavicular glands. Improved, became *free from pain* and lived one year and six months.

Case 534. - - F. Carcinoma, throat and neck. The neck became softer, swallowing easier and *pain less*. Lived for one year and one month after the first use of Ensol.

Case 546. - - M. Carcinoma, mouth and palate. Under Ensol *pain was relieved* and general condition improved with better swallowing. Lived four months.

Case 551. - - M. Carcinoma, testicle with involvement of inguinal glands. General condition improved, both
605 groins were better, *pain was controlled*. Continued better for several months then relapsed and died in six months.

Case 565. - - M. Carcinoma, larynx. Improved, became *free from pain* and lived eight months. Glands in the neck regressed and softened.

Case 579. - - F. Carcinoma, stomach. During the first two months treatment with Ensol there was definite improvement with a gain of seven pounds in weight and *relief of pain*. Lived in relative comfort for seven months.

Case 580. - - M. Epithelioma, right tonsillar area and glands in neck. A few days after treatment was started with Ensol *pain was completely controlled*. There was general improvement with better swallowing and appetite. One of the glands softened and was aspirated with further improvement. Was living six months later when reports ceased.

Case 583. - - F. Carcinoma, breast with induration in axilla and supraclavicular areas. After a month of treatment induration was less and *there was no pain*. Plaques on chest wall became softer and lighter. Lived nine months after first treatment with Ensol.

Case 640. - - F. Carcinoma, cervix. This was an advanced case in which *pain control* was rapidly established. Two years later the patient was still living and in fair comfort.

Case 675. - - F. Carcinoma, cervix. Advanced case with recto-vaginal fistula. Marked improvement with *relief of pain*. Lived for one year and six months.

Case 676. - - M. Carcinoma, bladder. Under Ensol treatment *pain and distress were completely relieved*.
606 Lived for seven months fairly comfortable.

Case 692. - - M. Carcinoma, rectum. Temporary improvement with *control of pain*. Lived for one year and one month.

Case A-30. - M. age 49. - Carcinoma, colon and rectum.
Feb./39. Exploratory operation. Found impossible to remove the growth. Colostomy. Biopsy,—carcinoma.

March 24/39. Ensol used.

May 4/39. Marked improvement with *pain relief*.

July 7/39. Able to return to work.

Aug. 29/39. Maintains weight, no increase in lesion.

Oct. 20/39. General condition satisfactory, gained four pounds, working eight hours a day.

Dec. 23/39. Still working and feels fairly well.

Case A-73. - M. age 70. - Carcinoma, sigmoid. Biopsy proof.

June/37: Exploratory operation. Liver secondaries. Mass could not be removed. Colostomy done.

April/38. Ensol used with systematic improvement and *relief of pain*. Regression of the mass.

Jan./40. Still holding very well.

Case A-34. - M. - Adenocarcinoma, rectum. Biopsy proof.

May/39. Found to be inoperable. Colostomy done.

July/39. Ensol used. Improved rapidly.

Aug. 19/39. Feeling quite well, *no pain*, weight up to 181 from 179 lbs.

Sept. 18/39. No complaints. Weight 184 lbs.

Nov. 15/39. Weight 192, better, *no pain*. Doing light work.

Jan. 11/40. Very well.

607 Case A-72. - F. age 52. - Carcinoma, sigmoid.
Biopsy proof.

June 1/38. Blood from bowel. Pain in abdomen.

June 15/38. Exploratory operation found far advanced carcinoma, with metastases in liver. No attempt at removal. Colostomy.

Sept. 14/38. Ensol used. Improved. *Pain relieved.*

Oct. 30/38. Gained in weight from 145 to 150 lbs. Eats and sleeps well.

Dec. 17/38. Feels well, further gain in weight.

March 4/39. Continues to improve.

March 18/39. Very well. Keeps *free of pain.*

Case A-88. - M. age 66. - Carcinoma, rectum. Biopsy proof.

Sept./38. First symptoms,—bowel obstruction gradually increasing.

Feb. 1/39. Examination found inoperable mass in rectum. Biopsy, carcinoma.

Feb. 4/39. Colostomy.

Feb. 10/39. Ensol used.

Feb. 24/39. Somewhat stronger, *free from pain*, eating and sleeping well.

March 24/39. Improved, is up and about the ward. *No pain.*

May 4/39. Satisfactory general improvement. Decrease in size of tumor mass.

July 4/39. Unchanged.

Sept. 13/39. Extension toward left buttock.

Oct. 27/39. Improved again. No further extension.

Case A-79. - M. - Carcinoma, sigmoid, annular growth with secondaries to gland and liver.

June/37. Abdominal pain for three months past. X-ray and barium showed obstruction in descending colon.

Laparotomy found annular growth. No attempt at removal. Lateral anastomosis to relieve obstruction. Involvement of mesenteric glands, nodules on inferior surface of liver. Since operation pain continued.

July 24/37. Ensol used.

Aug. 14/37. *Pain relieved.* Weight increased from 109½ to 120 lbs. Appetite improving, cachexia disappearing. Serous discharge ceased immediately after the use of Ensol.

Dec./37. General condition good. Continues to improve.

Case A-40. - F. - Carcinoma, sigmoid. Biopsy proof.

Feb./38. Exploratory laparotomy. Found impossible to remove the mass. Colostomy was done.

April/38. Ensol used. No noticeable improvement at first.

July/38. *Pain relieved.* Abdomen filled with new growth. Large cauliflower mass around colostomy opening. Ensol dosage increased. Prognosis estimated at ten days.

Nov./38. Patient alive and dosage again increased.

Dec./38. Patient is more comfortable. Some gain in weight and a definitely improved sense of wellbeing.

Case A-37. - M. - Carcinoma, colon, metastases in mesenteric glands and liver.

Aug./39. Exploratory laparotomy. Impossible to remove the mass. Section made of mesenteric lymph gland.

Oct. 2/39. Ensol used. Improved.

Dec. 1/39. Feels well, up and around, *no pain*, gained 13 lbs., drives his own car.

Jan. 20/40. Gained 5 more pounds. Looks well.

March 3/40. Continues very well.

March 13/40. Increased dosage produces tumor reactions. Very well.

609 Case A-49. - F. age 48. - Carcinoma, rectum. Biopsy proof.

Nov./35. Laparotomy revealed liver metastases. Colostomy done. Abdomen greatly enlarged, extension to uterus.

Oct./37. Ensol used. Followed *pain relief*, improved general condition but no change in abdominal mass. Pelvic induration was reduced and uterus became movable.

This was a far advanced case when taken on and was carried for 14 months.

Case A-66. - M. age 75. - Carcinoma, stomach, X-ray diagnosis.

Sept. 28/38. Found to be inoperable.

Nov. 5/38. Ensol used for palliation.

Nov. 23/38. Improved, *pain relieved*, eating and sleeping better. Has had tumor reactions.

Jan. 26/39. Died.

Case A-50. - M. age 69. - Carcinoma, stomach. Diagnosis clinical and X-ray. Had lost 50 lbs. in weight. Obstructive type vomiting, haematenesis.

May/38. Ensol used for palliation. Prognosis of only a few days. Vomiting and *pain relieved*, haemorrhage stopped.

Sept./38. Patient lived comfortably for four months and then died suddenly following massive haemorrhage.

Case A-67. - F. age 47. - Carcinoma, stomach. Diagnosis by X-ray.

July 15/38. X-ray examination showed involvement of cardiac end of stomach and oesophagus. Inoperable.

Oct. 19/38. Ensol used.

Oct. 24/38. At first pain and dysphagia increased.

Oct. 28/38. Improved, *pain less*.

610 Nov. 30/38. *Pain relieved to a great extent*. Increasing difficulty in swallowing. X-ray shows advance in size of growth. Doctor writes,—“strangely enough he is quite unable to get on without Ensol,—as soon as it is discontinued he starts to vomiting everything he eats. This is not a psychic effect as at one time when out of Ensol I substituted sterile water hypo with no effect whatever.”

Terminal report not given.

Case A-100. - F. age 63. - Carcinoma, stomach. Diagnosis by X-ray and exploratory operation.

Jan. 3/39. Vomiting and pain in upper abdomen. An elongated mass could be palpated in epigastric region, movable to the left.

Feb. 28/39. Ensol used. Marked *relief of pain*. Morphia almost discontinued.

May 17/39. Died. "Ensol did not have any effect on the carcinoma but it did materially *reduce the pain and discomfort.*"

Case A-65. - F. age 67. - Carcinoma, stomach, secondaries in liver.

June 25/37. Far advanced case of carcinoma with only a few weeks to live. Pain not relieved with opiates. Asked for Ensol in the hope of getting some relief.

June 27/37. Ensol used. After the second injection there was *decided decrease in pain*. This mitigation of pain continued till her death three weeks later.

Case A-71. - M. age 71. - Carcinoma, stomach, X-ray diagnosis.

May 25/39. Progressive condition over a year emaciation and gastric distress. Mass as large as the hand, very hard and immovable, extending to mid-abdomen down and to the right.

611 May 28/39. Ensol used for palliation. In two weeks the gastric symptoms and *pain were relieved*.

June 24/39. Feeling better, eating and enjoying his meals. Treatment continued but no report as to termination.

Case A-43. - F. age 61. - Adenocarcinoma, caecum. Biopsy proof.

Feb./38. Symptoms became severe with loss of 50 lbs. in weight. Exploratory laparotomy. No attempt to resect.

July/38. Ensol used. Rapid improvement, *marked pain relief*, gain of 7 lbs. in weight. *Morphia discontinued*.

Sept./38. Died suddenly.

Case A-78. - M. — Carcinoma, appendix with advanced secondaries throughout the abdomen.

Nov./35. Appendix removed and abdomen explored. Biopsy diagnosis,—adenocarcinoma.

May/36. Very painful mass attached to ileum.

Oct. 29/36. Part of this removed. Diagnosis,—carcinoma.

June 22/37. Ensol used. Some improvement.

Oct. 15/37. Some softening of the mass in right upper abdomen. Marked increase in appetite. Still needs morphia up to gr. $\frac{1}{2}$ daily, but usually less. Is bedfast.

Dec. 13/37. *Almost free from pain* and eating well. No termination report.

Case A-83. - M. - Carcinoma, prostate. Positive biopsy.

May/36. Far advanced case. Pain severe. Ensol used, no other treatment.

July 1/36. *Pain greatly relieved.*

Oct. 1/36. Looks better, has *very little pain*, is up and about his office. Local condition still shows hardness
612 around bed of prostate but general condition improved.

March/37. Died.

Case A-84. - M. age 65. - Carcinoma, prostate. Symptoms over five year period. No treatment except massage.

Nov. 11/37. Severe pain, weakness and fatigue, frequency. Ensol used. Only treatment. Given for palliation.

Jan. 18/38. *Pain controlled*, feels much better. Prostate not changed.

Sept. 15/38. *No pain*, appetite good, weight same. Prostate not further changed or enlarged.

Oct. 26/38. Not so well but wants treatment continued.

May 17/39. Growing weaker.

Termination not reported.

Case A-95. - M. age 29. - Carcinoma, spinal cord. Three years ago had injury to back.

Jan. 31/39. Operation,—laminectomy. Tumor found intrinsic in cord; could not be removed. Extremely severe pain in back. Opiates and analgesics of little value.

March 15/39. Ensol used in hope of relief of pain.

March 29/39. *Marked relief of pain.*

May 31/39. Daily injections of Ensol give comparative freedom from pain.

Aug. 19/39. Considerable *relief from pain*. To determine whether Ensol was the source of relief, injections of sterile water were used when the supply of Ensol was exhausted with the result that pain became much worse. Relief secured when Ensol resumed. No termination report.

613 Case A-108. M. age 67. - Carcinoma, oesophagus and cardiac end of stomach. X-ray and clinical diagnosis.

Oct. 28/36. Large filling defect at lower end of oesophagus and cardiac end of stomach; loss of 20 lbs. in weight in two months. Confined to bed in hospital.

Oct. 29/36. Ensol first used. Deglutition limited to liquids in small amounts, weight 106 lbs. Improvement began.

Dec./36. Taking all semi-solids with ease. Weight increased by 7½ lbs.; able to walk about. *No pain.*

Jan./37. X-ray report,—obstruction had not increased, growth smoother and less fungating.

Jan. 21/37. Went home. Reported taking the same food as the rest of the family.

April 27/37. X-ray report,—oesophageal obstruction has entirely disappeared, fungating carcinoma at cardiac end of stomach diminished in size and extent. No later report.

Case A-58. - F. age 69. - Carcinoma, uterus.

May 30/38. Laparotomy found posterior wall of uterus thick, hard and adherent to sacrum and to rectum. Removal of uterus impossible.

June 14/38. Ensol used. Gradual improvement.

Aug. 7/38. Slightly improved. *Less pain.*

Sept. 6/38. Feels fairly well. Some pain in sacral region.

Nov. 14/38. Greatly improved in health and strength. Some vaginal discharge. Goes to doctor's office daily for treatment.

Dec. 9/38. Soreness in lower abdomen. Doing her own housework.

Jan. 3/39. Has had a number of vaginal haemorrhages. No later report.

Case A-54. - F. age 48. - Carcinoma, pancreas. Biopsy proof.

614 June/37. Epigastric pain, distaste for food, flatulence.

Jan. 7/38. Entire pancreas enlarged and stony hard.

April 15/38. Ensol used. Pain aggravated for several hours after injection of Ensol. Appetite improving.

May 4/38. *Marked decrease in pain. Morphia reduced.* Pancreatic tenderness less. No decrease in size of mass. No termination report.

Case A - 45. - F. age 66. - Malignant retro-peritoneal cyst. 1937. Gradual development of abdominal tumor. Rapid development later.

Sept. 10/38. Laparotomy. Tumor found to be malignant cyst. Drain inserted.

Oct. 10/38. Ensol used.

Nov. 18/38. Doctor reports,—“When we started the Ensol she was practically in a dying condition. In a few days her general condition improved, got a better appetite. Drainage is much less but the tumor is very hard. *No pain or distress.*

No termination report.

Case A - 62. - F. - Carcinoma, bladder. Diagnosis at Toronto General.

Oct. 14/38. Large carcinoma in bladder. Considered inoperable. Severe pain in right side of abdomen; nausea and vomiting very troublesome.

Nov. 6/38. Ensol used for palliation. Improved. Morphia in massive dose not controlling pain and vomiting.

Nov. 20/38. *Morphia cut in half, less pain and vomiting.*
Is fairly comfortable.

Termination not reported.

615 Case A-60. - F. - Carcinoma, uterus. Advanced case.

May 22/36. Large mass in lower abdomen, cervix sloughed. Continued to lose weight, pain increased, loss of blood.

Aug. 2/36. Ensol used for palliation. Two days later the patient began to feel better. Appetite improved, slept well.

Aug. 14/36. Up in a chair, first time since May.

Aug. 20/36. Improves in every way. Mass in abdomen has diminished, *no pain, opiates discontinued.* On her feet several hours a day.

Sept. 1/36. Some nausea and vomiting.

Oct. 4/36. Doing very well, no nausea or vomiting.

Oct. 17/36. Vaginal haemorrhage, continued for a week.

Oct. 29/36. Died with brain symptoms, probably metastasis.

Case A-53. - M. - Carcinoma, oesophagus. Biopsy proof. Advanced case.

March 3/37. Diagnosis made at University Hosp., Ann Arbor. Medullary squamous cell sarcoma. Requiring a lot of morphia.

March 15/37. Ensol used for palliation. After third dose *morphia reduced.*

May 11/37. Failing but has had only three doses of morphia since Ensol was started.

May 25/37. "Died as expected. The benefit derived from Ensol in this case was the practical *elimination of morphia.*"

Case A-32. - M. - Carcinoma, prostate. Biopsy proof.

Oct./38. Resection. Diagnosis.

Feb./39. Taking 10 grs. morphia per day for pain.

616 April 28/39. Ensol used for palliation. *Pain controlled.* Morphia reduced to 1 gr.

June 20/39. Comfortable.

Case A-51. - M. - Carcinoma, prostate. Biopsy proof. Recurrence with involvement of rectum.

1933,—Resection with biopsy proof of carcinoma. Only partial removal.

Oct./38. Recurrence with involvement of rectum,—constant bleeding, tenesmus and severe pain, loss of weight, poor appetite and cachexia.

Aug. 30/39. Ensol used for palliation. After the fifth injection of Ensol he had the first night's sleep in weeks, due to *alleviation of the pain*; the bleeding ceased and appeared again only occasionally and then very little; gained some weight and felt very well.

No later report.

Case A-94. - F. - Carcinoma, vulva.

Aug. 16/37. Reported,—extensive advanced carcinoma of vulva, involving both labia majora and minora. Inoperable and radiation not feasible. Pain extreme.

Sept. 14/37. Ensol used for palliation.

Oct. 7/37. From the need of $\frac{1}{4}$ gr. morphia every three or four hours, *now reduced to small doses of codeine*.

Oct. 30/37. Died of uraemia. *Pain was relieved*.

Case A-103. - F. age 43. - Carcinoma, hard palate, extensive cauliflower growth. Having morphia $\frac{1}{4}$ gr. 3-5 times a day. Has had no radiation. Pain severe.

Sept. 1/37. Ensol used.

Sept. 28/37. "Almost miraculous the way she has improved." *Pain relieved*.

Dec. 7/37. Gained 27 lbs. in weight. Doing well.

617 Dec. 15/37. Very well.

June 21/38. Treatment discontinued for some time. Maintains her weight. *No morphia*.

Aug. 26/38. Doing fairly well. General health much better. Still some sloughing in the mouth. No later report.

Case A-104. - M. age 32. - Carcinoma, left ethmoid and orbit.

Jan. 1/38. Nasal obstruction and discharge. 7th nerve paralysis in July/38. Persistent headaches.

Aug. 6/38. Ensol used.

Sept. 30/38. Much improved, *relief of pain*, returned to work. Progress of growth seems to be retarded.

March 5/39. Died. *Relief of pain* was specially noted.

Case A-106. - M. age 65. - Carcinoma, oesophagus. X-ray diagnosis.

Feb. 28/39. Has had difficulty in swallowing for 18 months. Ensol used.

April 15/39. Taking and retaining more food. *Definite pain relief*. Feels more comfortable.

July 1/39. Died.

Case A-33. - F. - Carcinoma, uterus and rectum, metastases in liver.

Oct. 16/39. Ensol used for palliation. Improved.

Dec. 16/39. *Almost free from pain*. Weight maintained, getting about.

Jan. 15/40. Up and about, *free from pain*, gained 5 lbs.

Case A-62. - F. - Carcinoma, ovary. Advanced case with marked ascites.

Nov./37. First symptoms.

March/38. Ensol used. General improvement noted.

618 Feb. 2/39. Primary tumor larger but *no pain*, sleeps and eats well, not losing weight.

May 15/39. Tumor mass about the same, requires paracentesis every two weeks.

July 24/39. Had been very well till two weeks ago. Died. Heart attack.

Case A-105. - M. - age 68. - Carcinoma, oesophagus and stomach.

April 1/38. X-ray and clinical diagnosis. History of gradual development over a year.

Aug. 13/38. Ensol used. Has been unable to retain liquids.

Aug. 27/38. Feels better, taking liquids and soft food, no vomiting, *no pain*.

Oct. 14/38, *Free from pain*. Condition unchanged.

Nov./38. Died. Remained free from pain.

Case A-57. - F. - Carcinoma, uterus, secondaries to spine.

Aug. 1/38. Unable to control pain in spine with opiates. Asks for Ensol for palliation.

Sept. 3/38. Greatly *relieved of pain* since using Ensol. Opiates reduced by one-half and is far more comfortable.

Case A-81. - M. - Carcinoma, bladder, probable extension to rectum.

March/38. Found to be inoperable. Permanent suprapubic drainage. Ensol used.

Aug. 24/38. Condition no worse than six months ago. Has long intervals when *pain very much less*.

Sept. 14/38. Pulmonary embolism. Died.

Case A-86. - M. age 76. - Carcinoma, prostate; carcinomatosis in bones and lungs.

Nov. 2/36. Enlarged prostate found, nothing done due to poor physical condition and heart lesion. Malignancy suspected.

619 June/37. X-ray and physical examination at Presbyterian Hospital, N. Y., found widely scattered carcinoma of bones. Refused radiation treatment.

July/37. Ensol used for palliation.

Oct. 20/37. Decided symptomatic relief. Anxious to continue treatment because more comfortable on it.

Jan./38. Symptoms stationary.

March 3/38. Not going down hill as fast as expected.

July 26/38. Pale, weak and emaciated, bedridden, *not much pain*.

Date of termination not reported.

Case A-80. - M. age 63. - Epithelioma, bladder. Advanced case.

Feb./37. Laparotomy. No attempt at removal of growth. Ensol used. Bedridden, very weak, unable to move himself.

Aug. 27/37. A great change, stronger and better in every way. No evidence of secondaries. *Pain relieved.* Had been running a temperature since February. After the first week of Ensol this gradually dropped to normal.

Oct. 14/37. Progress slow but favorable. Out of bed for the first time since last spring. Complaining only of weakness. Urine remains clear.

Nov. 15/37. Sitting up and walking a little.

Dec. 27/37. Improving slowly.

Jan. 21/38. Not so well. Blood in urine.

No termination report.

"To date we have used Ensol on 16 cases and I have put a number of other people on it. Our results thus far have been beneficial in a marked degree in most cases and even those who have made an exodus *had definite relief of pain which was not obtained with ordinary methods of treatment.*"

620 "Carcinoma of cervix with frozen pelvis. Ensol treatment began April 29th at which time the patient was bleeding and suffering severe pain in back and hips and barely able to walk upright. Immediate improvement noticed *with complete disappearance of pain.* Weight increase from 126 to 131 lbs."

"At the onset of - - - 's treatment with Ensol we found that he was suffering from carcinoma of the prostate with severe pain in the legs and back. He has been on treatment for three months. Our clinical findings in this case showed that *after he had been on treatment for two weeks his symptoms of pain in the back and legs had diminished and at the present time he has no pains except of a very mild character.*"

"Carcinoma of the breast with secondaries in the chest and ribs. This patient receives considerable benefit from Ensol, in that *pain is absent, opiates reduced,* appetite improved, vomiting lessened and nutrition improved."

"It is interesting to note that during the two weeks period when Ensol was withheld all the symptoms of this pa-

tient were aggravated, namely, pain in the chest, coughing, vomiting, anorexia and, in addition, *the quantity of opiates was doubled* to give the patient relief. During this time patient appeared to slip back considerably in weight, strength and nutrition. Upon resumption of the Ensol treatment patient again quickly improved."

"The patients being treated are doing nicely. The last examination of - - - revealed white cell count 12,200, Hgb. 66. She is feeling well and has gained 28½ lbs. since treatment started. *She does not have to take any hypnotic nor any analgesic of any kind.* She always sleeps well and drives her car when she wants to."

621 "I have now two cases under treatment, in one of them I am getting *results which are almost spectacular as far as regards relief of pain.*"

"My patient has become quite comfortable and is *entirely free from pain.* In fact her only disabilities are the result of a two and a half or three months in bed or in a chair. She should rapidly return to normal with moderate exercise and beyond that I can only hope."

" died as expected. The benefit derived from Ensol in his case was *the practical elimination of morphia.*"

"Our Mrs. - - - has been much improved; she has gained two pounds in weight in the last three weeks. *She has no pain* and has vomited but three times since the 15th. I have just finished talking to her and she tells me that she feels fine."

Our patient - - - is doing fairly well. She vomited yesterday for the first time in two weeks. *She has had no pain for months.* Ensol has taken this woman from bed,—she was going from bad to worse and had taken to bed. In fact the first treatments were given at her home because she was unable to come to the office. That is, from 11/27/36 until 1/16/37, since which time, except in bad weather, she has come to the office for treatment. Frankly, I have never seen anything like it.

"In this case Ensol was very helpful and the patient rested better, ate better, had better bowel movements and *was free from pain throughout his illness*. The action of Ensol impressed me as being more like that of a cancer antitoxin."

" - - - continues to improve. She feels well and *has no pain*. She has gained eight pounds in all and eats everything."

"You will be interested in a report of one - - - who has now had Ensol injections for about four weeks. She
622 has had a radical right and left mastectomy for carcinoma of both breasts. Last March an X-ray showed rarefaction of the tuberosity of the ischium as well as the whole left hip joint. She soon was unable to step on the left leg, and then with such severe pain that she was bedridden. The use of the bedpan caused excruciating pain. I sent her to - - - hospital and applied Russell extension pull to the left leg. This relieved most of the pain and allowed us to care for her without distress. *The last two or three days the pain has entirely gone*. We have removed the traction apparatus. She is hungry and eats well. *We have discontinued morphia that she was getting in large and frequent doses*. The harassing cough that indicated lung involvement has disappeared. I do not pretend to say that this patient is recovered or will recover but the miraculous improvement is apparent to everyone and is certainly a credit to Ensol treatment."

"In regard to Ensol I must admit that it apparently accomplished three things: (1) Ensol seemed to prevent the tumor from enlarging and spreading so rapidly; (2) *Ensol kept the patient pain free. I did not give him any sedative or narcotics*; (3) It worked very well on his general condition."

" - - - is slowly progressing to the end. It is remarkable how she continues to live and *so free from pain with such an enormous involvement*. During my twenty years of practice I have never seen a case like her, with so much

involvement *and so little pain*. On the whole it is remarkable."

"This was a case of carcinoma of the mesentery including a portion of the small intestine. Your serum never had a chance but there was one marked change noticed,—*relief of pain*. *The morphia was halved in doses and as she progressed less was used and for the last week none.*"

623 "I am writing you in regard to - - - who has been under my care since May and is improving a great deal. X-rays reveal the growth to be about one-half the original size. Since my last letter he has gained about five pounds and *takes practically nothing to relieve pain.*"

"During the past three months - - - has received considerable *alleviation of pain and suffering*. After the initial administration of Ensol, *narcotics and sedatives were cut to the very minimum.*"

"- - - has been much improved since taking the serum. He has been *relieved of his pain* and has returned to work. The dosage has been worked up to 5.00 c.c. which seems to have controlled the progress of the growth."

"Re: - - - . The sarcoma is growing gradually but he has not lost any weight to speak of and he *has been free from pain*. That fact that *he is free from pain is to me very wonderful*, compared with others I have seen. There is no doubt that *Ensol is keeping him free from pain.*"

"Re: - - - . Died on Sept. 16th. The *Ensol did cause the severe pain to disappear completely*. The discharge from the sinus in the axilla dried up."

"Please forward more Ensol for - - - . The *increased doses have caused the pain to disappear.*"

"- - - is doing finely, slowly gaining weight, has *no pain or inconvenience* from his tumor and I think it is slowly decreasing in size. The condition is one which has shown marvellous results considering the type of tumor, as I have never known any treatment either surgical or medical that would control, even for a short time, a hypernephroma."

"I have been treating - - - with Ensol and am happy to report that *she has been greatly relieved in regard to pain.*

At the present time she requires *less than one-half*
 625 *the amount of opiates* and is far more comfortable than before using the Ensol. I know we cannot hope for any permanent cure in this case but we certainly *appreciate the relief of pain as it could hardly be controlled with opiates.*"

"From the cases on which I have used Ensol I feel that *it definitely relieves their pain* and that the patients feel better."

"My patient - - - on whom I had used Ensol died Sept. 28th. For the previous two weeks she had resisted the injections so we were unable to give it. I must say that I am convinced that it had a remarkable effect on her case as *she was free from pain ever since the Ensol treatment was started.*"

"I regret to inform you that - - - died about three weeks ago. The outstanding feature of her case was that *there was practically no pain*, which I attributed to the Ensol. It was of benefit in as much as it made her terminal days more comfortable."

"The patient receiving this treatment shows no diminution in the size of the tumor but *absolutely no pain.*"

"By the time Ensol was discontinued she was practically *free from pain.* Walked to the clinic, went to church and on June 18th X-ray films showed much improved bone shadows."

"The patient received increasing doses of Ensol for a period of three weeks, starting with 0.5 cc., with a daily increment of 0.4 c.c. This had the effect of *relieving completely the pain* and causing flattening of the uneven floor of the ulcer."

"- - - has gained 16 lbs. in weight, can eat a fair meal and *has no pain.*"

"Our patient - - - received 2 c.c. Ensol daily except Sunday from Nov. 9th to Dec. 6th when she died very

625 suddenly. Embolus. When she began Ensol *she was using a lot of morphia but the last two weeks of her life she required none.*"

" - - - continues on her 2.5 c.c. Ensol daily. She walks better and *has no pain in the pelvic bones now.* For a month she has been going up and down stairs, — something she had not done for six months previous."

" - - . On July 23rd injections of Ensol were started. He gained in weight and felt very much better. *Pain was greatly relieved, requiring nothing in the way of morphia.*"

"Mr. - - - is now starting his third year of Ensol treatment. The mass has become larger but growth is slow. There are a few small nodules protruding which are painful on pressure. The lumen through the mass has not lessened. He has lost very little weight and his color remains good. This latter case to me indicates definitely that Ensol retards the growth of the mass, *lessens pain* and distension as well as assisting in retaining weight. Metastasis is likely prevented."

"I came across another case of pelvic carcinoma (uterus involving the rectum) and I took the liberty of sharing one-half of - - - 's supply for my new patient. She was suffering intensely and only relieved by opiates. She is, of course, an incurable case but *for the past ten days has been entirely free from pain*, is eating quite well and is looking much better. I may add that Mrs. - - - is up and about daily and *free from pain* and has gained five pounds."

"Re: - - . I stopped the treatment for two weeks with this patient but she *had a return of her pains*, so I began again. She wanted to discontinue the Ensol because she did not believe it was helping her, *but found out it was.*

626 " - - . I have been treating her now for about ten days and she is showing a marked improvement in every way already. When I started her on Ensol she could not raise her head off the bed. She was not eating at all, was very nauseated and *had a lot of burning pain in*

the epigastrium. These symptoms have practically disappeared."

"I regret to report that this man died and I was unable to obtain an autopsy. The chief benefit derived from the use of Ensol in his case was the *relief from pain* and the comfort obtained."

"Re: - - - I can say definitely that there was no doubt a great deal of *relief of pain*. Her condition, *as far as suffering was concerned, was much more satisfactory after the injection of Ensol.*"

"In regard to - - - . I saw him about two weeks ago. Examination of the gland at that time showed a definite improvement in view of the fact that the gland was much softer, smaller and apparently movable. The urine was clear and *he was not suffering.*"

"- - - . Her condition seems to have improved since the treatment with Ensol was begun. She is *now practically free from pain* and the tumor mass over the end of the clavicle is slightly reduced in size."

"An inoperable case of carcinoma of the uterus. This patient had been *receiving for some time, 4 hypodermics of Morphine gr. 1/4 daily*. This is the seventh day of Ensol treatment and the seventh injection of Ensol. *There has been but one injection of morphine in all this time* and that was three days after the Ensol was started. The discharge has all stopped."

"- - - has improved greatly under the Ensol treatment. The tumor is smaller in size and *the pain has been entirely relieved.*"

627 " - - - is feeling very well and *has no pain*. He is much stronger, his shortness of breath is disappearing and his weight is now 114 lbs. There is no evidence of oedema."

" - - - was at my office this afternoon altogether a new person. The symptoms are much better, no more haemorrhagia, *no pains* in her legs, a good appetite, weight maintained at 124 lbs."

" - - - . Patient practically *free from pain*, able to move about on bed and get partly in sitting position, appetite good, in good spirits."

" - - - In the past two weeks this patient has improved under twelve injections of Ensol when *morphia in massive doses was not controlling pain and vomiting*. During the past few days under Ensol, *the morphia has been cut in half* and vomiting is controlled."

"Re: - - - . During the time this patient was without Ensol, pain in both sides of the chest had returned, cough and expectoration had increased, opiates had been doubled in quantity and the patient had become much weaker. In contrast to this, when under Ensol treatment, there was a sensation of fullness in the chest, *pain was absent, opiates were reduced to about one-half of the quantity previously required*, cachexia was absent and her strength greatly increased."

" - - - shows a gradual loss in weight and strength. She sleeps well, with *comparatively little pain while she is taking Ensol*; her appetite is fair and her colour good."

" - - - *died without any pain*. He continued with a good appetite until the day before he died and had no vomiting since the Ensol was used."

"I started to give - - - Ensol on April 16th and increased to 1.0 c.c. daily. Previous to this he was receiving
628 *morphine by mouth and required two to three hypos a week as well*. However, the only real improvement noticed was *his freedom from pain*. From the time he was given Ensol until his death, he required *no further morphine by hypo and very little*, if any, by mouth. It was certainly a hopeless outlook from the beginning, but during the time he received the Ensol his lot was a much happier one."

"Following exploratory operation his condition gradually became worse. He lost more weight and had a great deal of pain necessitating morphia. On July 23rd injections of Ensol were started. He gained a total of seven pounds in weight and felt very much better. *Pain was*

greatly relieved, requiring nothing in the way of morphia. He continued to feel better until two or three days before his death when he expired rather suddenly."

"Re: - - - Oct. 10th, *relief of pain quite noticeable.* Growth has not changed. Nov. 10th, 2 c.c. given twice daily. *Pain much relieved*, general condition the same, no change in weight. Growth the same."

"This patient, - - -, is as hoarse as ever but *has much less pain* and is encouraged and hopeful. As I am not expert with the laryngoscope I cannot report on anything but his general condition."

"Re: - - - When we started the treatment she was in a dying condition. A few days after we began to treat her with Ensol, her general condition improved, she got a better appetite and continued to improve. I finally worked the Ensol up to 3 c.c. daily. The retro-peritoneal tumor mass began to shrink about two weeks after we started treatment and continued to do so till now it appears to be enlarging again, but she feels much better and has a good appetite. The drainage is much less but the tumor mass is very hard.

She is not gaining in weight but probably has lost
629 some. *She has no pain or distress.*"

"- - - This is a severe case of cancer of the buccal area. It is a large open sore now. Patient cannot masticate, swallows with the greatest difficulty and suffers very much. I have given him one small bottle, 10 c.c., of Ensol. Since doing so he *is not in such pain* and the open sore does not look so angry. Deep X-ray therapy made it flare up very much."

"- - -. There has been no recurrence of diarrhoea. There is *complete absence of any pain* or pressure symptoms. There is no reduction in the size of the growth, nor, on the other hand, any appreciable gain. Weight remains at 171 lbs."

"- - - Carcinoma of the prostate, operated upon six years ago. Symptoms returned about fourteen months ago and by the time Ensol was used the rectum was involved and there was nearly constant bleeding, tenesmus and excruciat-

ing pain, loss of weight, appetite very poor and a cachectic look. After the fifth injection of Ensol the patient had the first night's sleep in weeks, *due to alleviation of the pain*; the bleeding ceased and then appeared again only occasionally and then very little. Appetite improved and he gained some weight and had a general feeling of wellbeing. Lately he is on the downhill again, partly explained by a kidney complication following a cold".

"Re: - - -. At first there seemed to be an improvement in her wellbeing but metastases occurred in the sternum and liver. Then she remained at a standstill for some time and later gradually became thinner. *She did not suffer during this stage of failing and did not require any sedative till the day before her death.* This quiet ending was materially

influenced by the amount of Ensol she received. I
630 had previously used colloidal gold without much change in her condition. Ensol appeared to slow the speed of the cancer down and kept her from suffering."

"I have under my care a case of prostatic cancer who has had three transurethral resections and also surgical removal of the left seminal vesicle. He is in good general condition but suffering from severe local pain. Previously, in using Ensol on - - -, *the relief of pain was very noticeable.* Could you send me a supply for this case?"

"The case was a gastric carcinoma. Ensol was started and unquestionably *relieved his pain* and made him much more comfortable during the last three weeks of his life."

"- - - Carcinoma of the mouth. My conclusions are:

1. Ensol certainly gave the man *relief from pain.*
2. Certainly caused the open sore to close from the size of that of a 25c piece to that of a 5c piece.
3. Did away greatly with the slime and offensiveness of the sore.
4. Did seem to halt the growth in the lymph glands involved.
5. Gave him his appetite but not his power to swallow,—too far gone before I saw him."

"Please forward me another supply of Ensol for Mr. - - - as I find it relieves his pain considerably. He looks well and his blood count is almost normal."

"- - - 's progress has been fairly satisfactory as far as pain is concerned. This is appreciably better. Her appetite is somewhat improved. The induration of the ligaments shows no particular change and there has been a little
631 more bleeding from the cervix. As you suggested I shall increase the dosage of Ensol."

"- - - has obtained marked relief from her pain by the use of Ensol. There has been no definite regression of the masses which are apparently metastatic carcinoma."

"Re: - - - Ensol certainly seems to *relieve the pain* and I am not sure that it does not check the growth, though it still keeps slowly spreading. On Feb. 3rd she fell and fractured her right forearm, so I stopped the Ensol for three weeks, but the pain in her head and neck became so severe that I once more started the Ensol. *The pain left her after the first injection* and has remained absent ever since."

"- - - This girl is in excellent condition. I reexamined her ribs and axilla yesterday and there is not a sign of recurrence. I thought at one time I could feel a gland in the right axilla. She has had the 'flu recently but has quickly regained her weight. *She has no pain.*"

"- - - Secondary carcinoma in dorsal and thoracic vertebrae, in both femurs and in all the bones of the pelvis.

March 1st,—Morphia gr. $\frac{1}{4}$ three to five times daily. Ensol 0.5 c.c. given.

March 9th,—Ensol up to 2.0 c.c. *Pains greatly reduced*, patient more cheerful and moves in the house freely.

March 10th,—From this date to April 14th, 2.5 c.c. were given daily and *patient enjoyed utmost comfort*. No sedative was administered after March 23rd.

April 7,—No Ensol for two days, *pain returning*. Morphia given twice in past two days. More Ensol sent for."

632 " - - - has been receiving 3.0 c.c. Ensol for some time but as the pain increased I have increased the dose to 3.0 c.c. the last few days. *The pain is now less.*"

" - - - has progressed to the point where the tumor mass has regressed 40%. *Her pain is not nearly so severe.* The prognosis in this case is more favorable."

" - - - About two months ago this patient complained of pain in the legs and side. X-rays taken showed appearance of cancer in bones of both legs and in two ribs. On April 10th I began Ensol and *pain subsided considerably.* Patient is confined to hospital and is getting Ensol daily.

" - - - Because of tenderness in the right adnexa and low grade fever, we did not dare to apply further radium therapy. Ensol was started on April 11th and given till May 15th. She has gained considerable weight, *has no pain* and seems to be stronger although the vaginal discharge continues."

" - - - was kept on Ensol until April 28th when she commenced to fail rather rapidly. She died on May 26th, the cause of death being secondary carcinoma in lungs and abdomen. She never at any time *complained of pain*, and I feel that the Ensol was a factor in her peaceful passing."

" - - - This patient *had relief from his pain* and did not require morphine while I was taking care of him."

" - - - Graduated doses of Ensol starting with 0.5 c.c., increasing to 2.0 c.c. daily and continued at that rate. Patient had no untoward reaction from this and *obtained relief from the pain with about the 10th injection.* She has continued well as far as suffering from pain is concerned.

The principal effect of the treatment has been the
633 *relief of pain* from the metastatic lesion to the 12th thoracic vertebra."

"Re: - - - Since receiving the fresh supply of Ensol, treatment was resumed after a lapse of five days, starting with 1.5 c.c. and increasing by 1/10 c.c. daily until we arrived at the dose previously given, 2.5 c.c. This was continued up to May 18th when pain again became troublesome. Again we increased by 1/10 c.c. until on May 23rd,

3.0 c.c. were given and this dose has been continued to date (June 8th). This has been *sufficient to control the pain*, although during the past week she had complained of 'neuritis.' This has not been severe enough to take morphine. It is interesting to note that during the period of five days *when no Ensol was given, it was necessary to display morphine rather freely. Since the resumption of Ensol, morphine has only once been taken.* We are again reaching the end of our Ensol. We apologize for troubling you so much, but I do feel that this patient's comfort in the past few months can be attributed to Ensol."

" - - - 's condition remains about the same. The tumor is slightly larger but he is not having *any serious amount of pain* or inconvenience from it. I think on the whole he is doing remarkably well. The Ensol certainly has held the tumor in check and he has lived longer now than I ever expected possible for him to do. His weight remains about the same, he sleeps well and has a good appetite. In fact, he says, he is feeling better than he did at the time we commenced the treatment over a year ago."

" - - - whom I have been treating for cancer of the stomach since last September, is nearly out of Ensol. For the past two or three months, I have been giving her only 5.0 c.c. twice a week. She has shown no untoward
634 symptoms, *no pain*, has a good appetite, is holding her flesh well and doing all kinds of housework. As long as she is doing well, I have not crowded it as much as you recommended at first."

" - - - is slipping. Her general strength has diminished considerably within the past six weeks. The open portion of the tumor is now nearly 10 cm. in diameter, and rather large masses of granular tissue have sloughed off without active bleeding. In spite of this apparent necrotic change, the area is practically free from offensive odor and *she is suffering very little pain.* In all my years of dealing with breast tumors, I have never seen one show this clinical course. I am convinced that Ensol is prolonging her life and it surely *has lessened the pain to a very marked degree.*

Up to date *she has had no narcotic, and very little sedative of any type.*"

"Carcinoma of the stomach. Ensol from April 29; report June 10/39. Patient *has very little pain* and has definitely felt better since he began Ensol."

"I have another case upon which I should like to use Ensol. Since the recovery of such a case as - - - I am all the more anxious to use it again. - - - has apparently completely recovered and has gained back all her former weight and strength, from 80 lbs. to 145 lbs. now, and does all her own housework. No more tumor mass in the abdomen or any other evidence of carcinoma. In addition *she broke herself of the morphine habit after taking it several times a day for about two years to control the pain.*"

"Re: - - - It has not been possible for me to give the injections as often as they should have been given but *she has obtained considerable palliation from the treatment.* If possible I should like to receive a further supply of Ensol."

635 "In the case of - - - whom I have been treating with Ensol I wish to report that he is retaining his weight, in fact has gained five pounds. *He has no pain* and the size of the tumor remains stationary."

"This is a blood sample from - - - three weeks after beginning treatment with Ensol. I was giving her up to 2 c.c. *She has been quite free from pain during the last week.*"

"Re: - - - . His response to treatment with Ensol during the last month has been phenomenal. He has a ravenous appetite, has gained 13 lbs. in weight and is rapidly gaining strength. He feels fine, *has no pain*, is up and around, drives his own car but has not attempted to do any work. He has been on Ensol for about six weeks."

"My case of advanced adenocarcinoma of the sigmoid continues to hold her own and *not suffer any pain* under Ensol therapy. About two and one-half years have now elapsed and we feel that this is really a remarkable time considering the unresectable lesion we found in the pelvis."

"- - - has really shown more improvement in the last

ten days than at any other time. No vomiting the last eight days, increase in weight, a better appetite, stronger, *no pain*, generally better in every way. Giving 5.0 c.c. Ensol daily, have eight days supply. Will be pleased to receive an additional supply."

" - - - has asked me to write to urge you to send Ensol for her as soon as it is available. *She has suffered much more pain since its discontinuance.*"

"The last examination of - - - revealed a more softened condition of the strictured area at the rectal-sigmoid junction with an ability to expel faeces with less effort and *no pain*. Manipulation caused a minimal amount of bleeding. However, there is a definite enlargement of the
636 uterine body and it is very firmly fixed in the pelvis, so much so that I was unable to produce any lateral movement and but a slight upward lift. It is distinctly palpable through the abdominal wall. Her general condition is fair, *she has little pain*, although she had lost weight but has regained a few pounds."

"Peritonescopy was performed Sunday. A malignancy of the transverse colon with carcinomatous transplants to the peritoneum was discovered. The lesion has evidently been inoperable for some time. However, the patient *does not complain of much pain and the Ensol must be given credit for considerable palliation.*"

"Re: - - - . Only enough Ensol to last six days. Gradual improvement, stronger, more cheerful, far less vomiting; able to sit up longer each time, weight same, more sleep. Cough very changeable, never severe. *No real pain in the pelvis*, slight stiffness in the right hip. Please send further supply. Now giving 5.4 c.c. daily."

"Re: - - - was in lots of pain when I found him, was taking two $\frac{1}{4}$ gr. tablets of morphine a day. In five days he was *free from pain and never took another bit of morphine*. As long as he could take sufficient nourishment he gained strength and courage."

"Re: - - - . Last week I discontinued the Ensol for four days to determine the effect upon the pain, as well as the

growth. There was little effect or change in the growth but *the pain became terribly bad*. I then began 2.0 c.c. Ensol doses daily. Yesterday *the pain began to subside* and the size of the mass decreased about one-third of what it had been. This morning she is resting very nicely with less than half the morphine."

637 "The supply of Ensol for - - - is nearly exhausted and am now making application for a further supply. I may add that she is *almost free of any pain* and is very grateful on that account. She is maintaining her weight and is about daily in spite of the fact that she had metastasis in the liver before treatment began."

III. MATERIAL RELIED ON BY APPELLEE.

A. Published Notes and Papers.

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1. Note by Gye.

Appellees' Exhibit 1B.

639 *American Journal of Cancer, Jan. 1936*

Treatment of Cancer by Proteolytic Enzymes, W. E. Gye.
Brit. M. J. 2: 760, 1935.

The following note concerning the treatment described in the preceding abstract appears in the Correspondence column of the British Medical Journal:

“In the Journal of the Canadian Medical Association for October, 1935 (p. 364), an article entitled ‘The Study and Treatment of Cancer by Proteolytic Enzymes,’ by Dr. H. C. Connell, appears. In this article reference is made to the fact that the Imperial Cancer Research Fund had been asked by Dr. Connell to investigate experimentally his claim to have discovered a method of killing cancer cells *in vivo*—potentially a cure for cancer. We have prepared from mouse tumours, in accordance with directions received, the solutions which Dr. Connell calls ‘ensols,’ and have tested these “ensols” on the appropriate tumors of mice. In no case has the growth of a tumor been checked or affected in any way.”

W. E. Gye.

2. Paper by Rusch and Preston.

Appellees' Exhibit 1C.

641 Proc. Soc. Exp. Biol. and Med., June, 1936,
The Effect of Filtrates of *Cl. histolyticum* upon the Growth
of Animal Tumors.

Harold P. Rusch* and William S. Preston. (Introduced by
Walter J. Meek.)

From the Departments of Physiology and Medical Bacteri-
ology, University of Wisconsin.

Connell¹ has recently reported a small series of cancer patients who, he believed, were benefited by the use of proteolytic enzymes, which were obtained by the growth of *Cl. histolyticum* upon tumor tissue. Torrey and Kahn² had previously produced an enzyme by the growth of *Cl. histolyticum* on a 3 to 4% peptone meat infusion broth and following the injection of this material into the Flexner-Jobling rat carcinoma, reported a 50 to 75% cure. Parenteral injections were of no value. Des Ligneris,³ in quoting some earlier work of his along similar lines, reports results of an entirely negative character. Gye⁴ was unable to confirm Connell's results, using mice as test animals.

The experiments here reported were done for the purpose of testing the effect of certain bacterial filtrates prepared according to the method of Connell upon the rate of growth of 2 animal tumors, whose characteristics are well known and thoroughly established. According to Connell's statement, such solutions should contain proteolytic enzymes.

Preparation of the bacterial filtrates. Three types of tissue were used separately as sources of media for the
642 production of the filtrates: the viable portions of the
Flexner-Jobling rat carcinoma, mouse sarcoma No.

* Jonathan Bowman Cancer Research Fellow.

¹ Connell, Hendry, *Canadian Med. J.*, 1935, 33, 364.

² Torrey and Kahn, *J. Cancer Research*, 1927, 11, 334.

³ Des Ligneris, *Brit. Med. J.*, Dec. 28, 1935, p. 1280.

⁴ Gye, *Brit. Med. J.*, Oct. 19, 1935, p. 760.

180, and rat muscle, the latter serving as a control. These tissues were removed with aseptic precautions, and about 15 gm. of each tissue placed in separate Erlenmeyer flasks to which normal saline was added in the proportion of about 10cc. to one gram of the tissue. The media were then inoculated with pure culture of *Cl. histolyticum* and incubated at 37.5° C. under anaerobic conditions for from 4 to 6 days until the contained tissue had become disintegrated. The liquid contents of the culture were then filtered first through filter paper and then through Mandler candles, following which each was placed in a sterile container and kept in the refrigerator until used.

The 3 different solutions obtained by this procedure will be referred to as "rat tumor filtrate," "mouse tumor filtrate," and "rat muscle filtrate." These solutions were given by one of 3 routes: intramuscularly (thigh muscles), intraperitoneally, or directly into the tumor in 0.5 cc. doses daily in rats and 0.2 cc. amounts every other day in mice, continuing until the animals died. In preliminary work it was found that larger, more frequent doses in mice would result in a loss of weight and early death due to toxicity. The rat tumor filtrate was given to rats and the mouse tumor filtrate to mice, except for 6 animals of each species, where cross injections were performed to test for specificity of the solutions. The rat muscle filtrate injected into the thigh muscles of the rats also served to detect any proteolytic action on normal tissue. In the rats injected directly into the tumor, only animals were used which had previously been inoculated with tumor material in 2 sites. Injections were made into one tumor with the filtrate and with normal saline into the opposite one.

Injections were begun only after the inoculated tumor cells were apparently established and by the size of the growing mass it could be more readily determined which tumors would be likely to grow and not regress spontaneously. This was about a week after the inoculation in the mice and about 3 weeks in the rats. All tumors were mea-

sured at weekly intervals. An inbred strain of mice, "C-57" (black) of Little, susceptible to sarcoma No. 180, and a closely inbred strain of stock rats having about an 85% susceptibility to the Flexner-Jobling carcinoma were the animals used.

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TABLE I.

Animal used	No. animals in exp.	Source of bacterial filtrate	Site of injection	Amt. injected	Average length of life (days)
Rat	10	Flexner-Jobling rat carcinoma	Into tumor	0.5 cc. daily	28
"	19	Flexner-Jobling rat carcinoma	Intramuscularly	"	44.8
"	15	Normal saline solution	"	"	50
"	6	Flexner-Jobling rat carcinoma	Intraperitoneally	"	40
"	6	Normal saline solution	"	"	45
"	5	Rat muscle	Intramuscularly	"	38
"	6	Mouse Sarcoma No. 180	"	"	41
Mouse	15	Mouse sarcoma No. 180	Into tumor	0.2 cc. every other day	9
"	15	Normal saline solution	" "	"	7
"	19	Mouse sarcoma No. 180	Intramuscularly	"	11
"	18	Normal saline solution	"	"	10.1
"	18	Mouse sarcoma No. 180	Intraperitoneally	"	5.3
"	15	Normal saline solution	"	"	12
"	6	Flexner-Jobling rat carcinoma	Intramuscularly	"	9

In vitro tests were done to test for proteolytic enzymes and for any specificity which they might have. Pieces of rat tumor, mouse tumor, and rat muscle were removed with aseptic precautions and placed in test tubes to which 5 cc. of one of the 3 filtrates was added. Five tubes were used for each test. These were then placed in an incubator for one week and observed for tissue disintegration at the end of this time.

No inhibition in the rate of tumor growth was noted in any of the treated animals as compared with the controls

except when the mouse tumor filtrate was given intraperitoneally to mice. Following this procedure, the tumor growth was halted, the mice lost weight, appeared toxic, and died in a few days. That the solution was toxic for normal animals was demonstrated by the fact that when somewhat larger doses, 0.4 cc., were given intraperitoneally to healthy mice, the animals died in from 2 to 6 days. No difference in the number and frequency of metastases were noted in the treated and control animals.

The variation in length of life noted in the different experiments, except in the group mentioned in the preceding paragraphs, is not considered of any significance, because of the small number of animals used in each series.

The early breakdown and necrosis which occurs in a tumor following the injection of many types of solutions directly into it appeared to be much more severe in the tumors in which the solutions were given as compared with those in which normal saline was used. However, the tumors continued growing at parts not reached by the solution, and this finding could be determined only, in degree, by comparative observation.

Sections of thigh muscles which had been injected with the solutions used were removed at autopsy and examined for histological changes. While evidence of inflammation was present in almost all, and infection in several, no evidence of a proteolysis could be observed by this method.

In the *in vitro* tests for proteolysis, none of the tissues suffered a disintegration such as that noted in those in which *Cl. histolyticum* is growing. Only softening of the tissues in varying degrees was noted. This was probably due to autolysis, since it was not more pronounced than that seen in the saline controls. According to this method of testing, we were unable to demonstrate any enzymatic activity in the filtrate.

NOTE: Since this paper was written, Pommerenke (*J. Am. Med. Assn.*, 1936, 106, 1654) has reported results of a negative character in the use of similar bacterial filtrates tested upon the Brown-Pearce rabbit epithelioma.

Conclusions. The solutions prepared according to the method of Connell and tested upon mouse sarcoma No. 180 and the Flexner-Jobling rat carcinoma were without any effect in prolonging the life of the animals, in preventing or decreasing the number of metastases or in inhibiting the rate of tumor growth.

3. Paper by W. T. Pommerenke, M.D.

Appellees' Exhibit 1D.

Effect of Injection of Bacterial Filtrate on Brown-Pearce Rabbit Epithelioma

645 *From Journal A. M. A.—May 9, 1936*

The employment of bacteria or their products in the treatment of malignant disease is not new. One need only refer to the work of Coley,¹ who for some forty-five years has reported favorably on the use of bacterial preparations in certain neoplasms. More recently Beebe and Tracy² were able to observe regression and disappearance of transplanted tumors in dogs that had been given injections of bacterial filtrates. Complete destruction of a transplantable mouse tumor was produced by Shear³ in a high percentage of cases with filtrates of *Bacillus coli*. It is not my purpose here to review the rather extensive literature since it instigated the present study. Connell reported that symptoms of some patients suffering with carcinoma could be ameliorated by the administration of certain bacterial that has accrued on this general subject. However, reference must be made to the recent publication of Connell,⁴ filtrates containing enzymes, which he calls "Ensols."

From the Department of Obstetrics and Gynecology, University of Rochester School of Medicine and Dentistry.

1. Coley, W. B.: Contribution to the Knowledge of Sarcoma, *Ann. Surg.* 14: 199-220, 1891; The Treatment of Malignant Tumors by Repeated Inoculations of Edysipelas, *Am. J. M. Sc.* 105: 487-511 (May) 1893; The Treatment of Sarcoma of the Long Bones, *Ann. Surg.* 97: 434-460 (March) 1933.

2. Beebe, S. P., and Tracy, Martha: The Treatment of Experimental Tumors with Bacterial Toxins, *J. A. M. A.* 49: 1493-1498 (Nov. 2) 1907.

3. Shear, M. J.: Studies on the Chemical Treatment of Tumors. *Am. J. Cancer* 25. 66-88 (Sept.) 1935.

4. Connell, H. C.: The Study and Treatment of Cancer by Proteolytic Enzymes, *Canad. M. A. J.* 33: 364-370 (Oct.) 1935.

These Ensols Connell prepared by inoculating with *B. histolyticus* a tube containing cancer tissue immersed in physiologic solution of sodium chloride. The cultures were incubated anaerobically at 37.5 C. for from four to six days, during which time the cancer tissue was digested presumably by ferments generated by the bacteria and specific for the type of cancer protein provided in the medium. The sterile filtrate obtained by passing the fluid through a Berkefeld candle was found to produce "much more rapid lysis of the cancer cells than took place in control tubes undergoing sterile autolysis." According to Connell's statements, clinical improvement of certain patients having carcinoma resulted from the injection of these Ensols. The growth of visible tumors was checked with softening and absorption. Patients having pain as a prominent symptom obtained relief with Ensol and were enabled to get along with a diminished dosage of sedatives. As far as is known to me, Gye⁵ is the only one to have published subsequently experiments similar to those of Connell. He was unable to observe any effect of the injections of Ensol on the growth of mouse tumors.

Because of obvious restrictions incidental to the use of human material, the present study was undertaken on animals, in the hope thereby of gaining accurate experimental information on the mode of action and on the effects of similar bacterial filtrates. The Brown-Pearce rabbit epithelioma of the testicle would appear to be a particularly suitable test tumor and was used in these experiments. Its genealogy and biologic behavior are well known. It is a highly malignant animal tumor which, unchecked, runs a rapidly fatal course in a large proportion of cases.

METHOD

Inoculation of Animals.—Unless recorded to the contrary, the tumor tissue used for inoculation and for the preparation of the bacterial filtrate was obtained from

5. Gye, W. E.: Treatment of Cancer by Proteolytic Enzymes, Brit. M. J. 2: 760 (Oct. 19) 1935.

nontreated and otherwise normal rabbits. This viable tumor tissue was removed either from the primary tumor growth or from a metastatic nodule. Tissue from one to four representative regions of the tumor mass was prepared for microscopic examination. Other tissue from the same region was minced with scissors until the individual particles were about the size of wheat grains. These were handled under aseptic precautions throughout and introduced with a trocar into the central portion of the testis, two or three such particles being inoculated into each rabbit. This is the standardized technic employed for more than three years in the division of radiology⁶ and has been used in the inoculation of more than 1,000 rabbits. The rabbits in this series which had received such tumor inoculation were divided into two almost equal groups, one half receiving the bacterial filtrate, the other serving as controls.

Preparation of the Bacterial Filtrate.—The bacterial filtrate was prepared according to the directions of Connell for the production of Ensol. Masses of tumor tissue were removed aseptically from rabbits anesthetized with ether. As much as possible of the adjacent tissue, either from the site of the primary tumor or from a metastatic nodule, was carefully dissected away, so that the remaining tissue was quite homogeneous, thus fulfilling the supposed requirement that only one type of protein be present in the medium. This tumor tissue, which was of the same type as that used for inoculation of other rabbits, was then immersed in physiologic solution of sodium chloride, the proportion of tissue to the solution being approximately 1:10. After the mediums were inoculated with *B. histolyticus*⁷ the culture was rendered anaerobic with a layer of sterile petrolatum and incubated at 37.5 C. for from five to eight days. During this time lysis of the tissue could be readily observed. Fibrous tissue and other undigested residue settled

6. The author is indebted to Dr. Stafford Warren and Mr. Otto Sahler, Division of Radiology, Department of Medicine, of the University of Rochester School of Medicine and Dentistry, for supplying the original stock tumor and for instruction in the method of making the inoculations.

7. American type culture collection No. 611.

out. The supernatant fluid was passed through a Berkefeld candle, and the filtrate, after having passed the test of sterility in this final form, was now ready for injection. It will be noted that this filtrate was prepared without exception from the precise type of tumor tissue with which the rabbits were inoculated. Furthermore, rabbits 78 and 81 received injections of filtrate prepared from tumor tissue removed from their own bodies. A sizable colony of rabbits with tumor was available to supply tissue for fresh filtrate. At no time was the filtrate more than 16 days old when injected.

Injection of Filtrate and Further Care of Animals.—

Preliminary injections of 0.2 cc. of the filtrate were 646 given under the skin of the ear to determine possible toxicity or other deleterious effect. It was soon learned that rabbits could tolerate with impunity dosages as large as 4 cc. given intravenously or subcutaneously. Larger doses were not given, and it is believed that no untoward effects have immediately followed any of the injections. The usual procedure was to inject the rabbits daily, the intravenous and subcutaneous routes being used on alternate days. The routine dosage was 0.6 cc. The rabbits were kept in individual cages and received a diet of oats, cabbage and alfalfa. Tap water was provided ad libitum. Aside from the matter of injections of the filtrate, the controls received the same treatment as did the experimental animals. The animals were periodically weighed, the weights being considered an index of their general condition. At frequent intervals calipers were used to measure the rate of growth of the primary tumor, graphic records being kept. Note was also made of the appearance and growth of metastases. When in the course of events, both in the treated and in the untreated group, cachexia supervened as a result of the malignant growth and it appeared that the animal would in all probability die within a few hours, the animal would be killed, so that fresh tissue might be available for microscopic study. When this occurred, the term "killed—extremis" was applied in the accompany-

ing tables. Even with this precaution, an animal would occasionally die during the night. However, in all cases autopsies were promptly performed. The tissues were preserved in Zenker's fixative and stained with the usual hematoxylin and eosin. We were thus enabled to accumulate a fairly complete series of slides of tissues coming from the control and the injected groups, as well as in cases in which biopsies were taken from the same animals before and after treatment.

TABLE 1.—*Effect of Injections of Filtrate on Rabbits Previously Inoculated with Tumor Coming from Untreated Hosts.**

	Rabbit Sup- plying Tumor	Rabbit Re- ceiving Tumor	Time After Tumor In- oculation when Injections Began, Days	Total Number of Injections	Longevity Following Inocula- tion with Tumor, Days	Comment
Experimental group A	899	74	17	41	58	Died from tumor metastases
	899, 74, 75 and 207	76	17	138	155, 113, 97 and 43	Living; (?) im- mune to tumor
	899	77	17	92	109	Killed—extremis
Control.....	899	73	..	..	64	Killed—extremis
	899	75	..	..	42	Killed—extremis
	899	78	77	8	85	Died from tumor metastases*
Experimental group B	898	79	14	80	94	Died from tumor metastases
	898	80	14	138	152	Living; tumor growth appeared arrested
	898	81	66	8	72	Died from tumor metastases*
Control.....	898, 74, 75 and 207	82	..	..	152	Living; (?) im- mune to tumor
Experimental group C	903	93	13	61	74	Died from tumor metastases
	903	94	13	31	44	Killed—extremis
	903	98	13	44	47	Killed—extremis
Control.....	903	95	..	..	96	Killed—extremis
	903	96	..	..	129	Living; tumor growth appeared arrested.
	903	97	..	..	129	Living; tumor growing

*Recipients of the tumor had had no preliminary treatment. Injections were continued to date or until the animals died.

TABLE 2.—*Experiment 2.**

	Rabbit Sup- plying Tumor	Rabbit Re- ceiving Tumor	Number of Pro- phylactic Injections	Total Number of Injections	Longevity Following Inocula- tion with Tumor, Days	Comment
Experimental group D	75	76	25	138	113	Living; (†) im- mune! no take
Control.....	75	82	..	..	113	Living; (†) im- mune! no take
Experimental group E	903	88	10	58	48	Died from tumor metastases
	903	89	10	141	131	Living; tumor growth static or regressive
	903	90	10	71	61	Killed extremis
Control.....	903	87	..	..	131	Living; tumor growth static or regressive
	903	91	..	..	113	Died from tumor metastases
	903	92	..	..	75	Died from tumor metastases

* In these groups, tumor coming from untreated hosts was transferred to rabbits having had preliminary or prophylactic injections of the filtrate. Injections were then continued to date or until the animals died.

EXPERIMENTAL STUDY

The almost invariable finding that variation is the rule in biologic response certainly must be regarded in the interpretation of phenomena pertaining to cancer growth and destruction. Innate resistance to cancer is probably not constant in different individuals or animals. Numerous factors doubtless determine whether or not a fragment of cancer tissue will take root and thrive within a new host. The behavior of a large number of transplants of cancer will have to be observed before an entirely satisfactory basal or standard response can be determined or anticipated. But even allowing for these variables I believe that the present series of experiments will permit of certain deductions. Only a portion of the observations lend themselves to statistical treatment. Primarily for convenience, however, pertinent data have been arranged in tabular form. As criteria for the determination of the effects of

647 injection of the bacterial filtrate on the growth of the Brown-Pearce rabbit epithelioma, the following were used:

1. The percentages of takes.
2. The rate of growth of the primary tumor.
3. The development of metastases.
4. The regression or disappearance of the tumor.
5. The longevity of the animal after inoculation with tumor.
6. The microscopic appearance of the tissue.

Table 1 summarizes the first experiment. Injections of filtrate were started on the seventeenth, fourteenth and thirteenth days following the inoculation of three groups of rabbits with the tumor fragment. Rabbit 76 appeared to be immune to this tumor, since four attempts at establishing the tumor transplants were unsuccessful. Rabbit 78 was originally selected as a control. However, when the tumor growth was 77 days old and metastases were noted in the pelvis, the primary tumor was removed and the rabbit then given injections. Eight injections of filtrate prepared from this rabbit's own tumor apparently did not materially alter the fatal course of the disease. In group B the tumor growth in rabbit 80 had become apparently static. The animal remained in good clinical condition after 138 injections of filtrate, even though metastatic nodules persist. The primary tumor has diminished somewhat in size but still persists. Rabbit 81, which as rabbit 78 originally served as a control, received eight injections of an isofiltrate without apparent effect. Control rabbit 82 in this group is apparently immune to this type of tumor, since he withstood four attempts at establishment of the tumor. When one compares the longevity of the rabbits in the three groups of experiment 1, it is apparent that the injected animals did not seem to possess a striking advantage over the controls.

In experiment 2 (table 2) a group of rabbits was given a "prophylactic" or preliminary course of intravenous and subcutaneous injections of filtrate. After this the rabbits were given inoculations with the tumor taken from untreated animals having actively growing tumor. Subsequent injections also were given, the total number of injections being indicated in the table. The results in group D may well be thrown out. The tumor transplants coming from rabbit 75 apparently fell on unfertile soil, as rabbits 76 and 82 have repeatedly shown themselves to be immune. In group E, however, it will be noted that the span of life of the rabbits receiving the injections was not prolonged.

Another experiment consisted of inoculating three rabbits with tumor from a rabbit that had received injections of filtrate on the preceding eight days. No further treatment was given these three animals. The transplants of tumor took in every case. Today, seventy-one days following the inoculation, two rabbits are showing progressive cachexia. In the third rabbit the tumor growth is apparently arrested or is perhaps even regressing, although the primary tumor still measures 3 by 2.5 by 0.5 cm. in its various diameters.

TABLE 3.—*Experiment 3.**

	Rabbit Supplying Tumor	Number of Injections of Filtrate to Rabbit Supplying Tumor	Rabbit Receiving Tumor	Injections Given to Rabbit Receiving Tumor		Longevity After Inoculation with Tumor, Days	Comment
				Before Inoc- ulation with Tumor	Total Number of Injections		
Experimental group F	74	41	76	41	138	97	Living (♂) immune to tumor
	74	41	19	25	99	74	Killed—extremis
	74	41	99	25	122	97	Living; tumor growing
	74	41	100	25	99	74	Killed—extremis
Control.....	74	41	82	..	..	97	Living; (♂) immune to tumor
	74	41	201	..	..	97	Living; tumor growing
	74	41	202	..	..	68	Died from tumor metas- tases
Experimental Group G	94	31	12	34	99	65	Killed—extremis
	94	31	13	34	122	88	Living; tumor growing
	94	31	15	34	117	83	Died from tumor metas- tases
Control.....	94	31	203	..	..	56	Killed—extremis
	94	31	204	..	..	43	Died from tumor metas- tases

* In these two groups, tumor from two rabbits which had received courses of injections of filtrate was inoculated into other rabbits which had already received preliminary or prophylactic injections of filtrate. Injections were then continued to date or until death of the animals.

TABLE 4.—*Experiment 4.**

	Rabbit Supplying Tumor	Number of Pro- phylactic Injections	Total Number of Injections	Rabbit Receiving Tumor	Number of Injections to Rabbit Receiving Tumor	Total Number of Injections	Longevity After Tumor Inoculation, Days	Comment
Experimental group H	90	10	71	205	19	89	70	Living; tumor growing
	90	10	71	206	19	89	70	Living; tumor growing
	90	10	71	207	19	45	26	Died of tumor metastases
Control.....	90	10	71	211	..	..	70	Living; (§) immune
	90	10	71	212	..	..	70	Living; tumor growing
	90	10	71	213	..	..	62	Died of tumor metastases

* In the experiment tabulated here, three rabbits which had received prophylactic injections of filtrate were inoculated with tumor taken from a rabbit which had had ten prophylactic injections and sixty-one subsequent injections. Injections into the three rabbits were continued to date or until death of the animals.

In experiment 3 (table 3) tumor tissue was removed from rabbits that had just received a course of treatment consisting of daily injections (forty-one and thirty-one) of filtrate. This tissue was immediately transplanted to two other groups of rabbits, which had then just completed a course of preliminary or prophylactic injections of filtrate. The injections were then continued without interruption to date or until the animals died. Examination of table 3 shows that the length of life or condition of the rabbits was not significantly altered by the injections.

In experiment 4 (table 4) ten preliminary or "prophylactic" injections of the bacterial filtrate were given to rabbit 90 on the days immediately preceding inoculation with tumor. On the sixty-one days following the inoculation with tumor the injections were continued, the rabbit receiving in all seventy-one injections. Tumor fragments from this rabbit were now transplanted into six rabbits. Three of these, rabbits 205, 206 and 207, had by this time already received nineteen prophylactic injections. The injections of filtrate into these three rabbits were continued to date or until the death of the animal. At present four of the six rabbits in this group are living. In two of the treated rabbits the tumors and metastases are apparently still growing. One treated animal died on the twenty-sixth day following inoculation with tumor. In the control group one rabbit died of tumor metastases on the sixty-second day. Examination of table 4 will show that no apparent protection was conferred on the rabbits receiving the filtrate.

In experiment 5 the tumor was first passed through two hosts that had received injections of the filtrate before and after the inoculation with tumor. The first of these, rabbit 90, had received ten prophylactic injections and sixty-one injections after the inoculation with tumor. Tissue from this rabbit was then transplanted into rabbit 207, which by this time already had received nineteen prophylactic injections. Injections were continued in this rabbit, twenty-six

more being given. Tumor from the second rabbit (207) was then inoculated into the five rabbits listed in table 5, which summarizes this experiment. If one discounts the case of rabbit 215, in which the tumor failed to take, it will be noted that the two rabbits which received the injections are apparently in the same clinical condition as are the two untreated controls. The tumor has thus passed through three generations of treated hosts and at the present time appears to be capable of unchecked growth, since all the rabbits in which the tumor took have growing primary and metastatic tumors, even while the daily injections are being continued.

Further evidence to indicate that injection of the filtrate does not alter significantly (1) the number of takes, (2) the percentage of tumors the growth of which has become static or regressive, (3) the progressive growth of the tumors and (4) the number of animals dying of tumor metastases is illustrated in table 6. This table presents a general summary, without regard to the particular type of treatment in the various experiments. Rabbits 78 and 81 might perhaps be more properly listed under the non-treated column, as they received only a small number of injections before they died of tumor metastases. Since the number of controls practically equaled the number of injected animals, the striking parallelism in the clinical course of the various groups seems significant.

Examination of Tissue.—No difference could be observed in the growth habits of the tumor in the treated and the nontreated animals. The usual mode of dissemination of the tumor inoculated in the testis is by extension along the spermatic cord to the pelvis. Metastatic nodules are frequently found in the retroperitoneal and omental glands. The kidneys were secondarily involved in a large percentage of cases. Metastases were also commonly found in the liver, spleen, lungs and mediastinum. Less often they are found under the skin or in the eyes. The abdominal and renal metastatic tumors are readily palpable in the

living animal. Frequently the larger tumors become necrotic in their centers, presumably because of inadequate blood supply. Special pains were taken to observe whether more necrosis occurred in the treated or in the nontreated groups of animals. No constant difference could be found. Microscopic preparations likewise failed to reveal any recognizable and characteristic morphologic changes as a result of the injections. In no case did the microscopic picture present evidence that the treatment destroyed the actively invasive appearance of the tumor.⁸

8. The author is indebted to Dr. William B. Hawkins, associate professor of pathology, University of Rochester School of Medicine and Dentistry, for reviewing with him all the microscopic slides prepared in connection with this study.

TABLE 5.—*Experiment 5.**

	Rabbit Supplying Tumor	Number of Pro- phylactic Injections	Total Number of Injections	Rabbit Receiving Tumor	Number of Prophylactic Injections to This Rabbit	Total Number of Injections	Longevity After Tumor Inoculation, Days	Comment
Experimental group I	207	19	45	214	13	56	43	Living; tumor growing
	207	19	45	215	13	56	43	Living; (1) immune; no take
	207	19	45	216	13	56	43	Living; tumor growing
Control.....	207	19	45	217	..	..	43	Living; tumor growing
	207	19	45	218	..	..	43	Living; tumor growing

* The P and F₁ generations of the hosts having tumor received prophylactic injections prior to inoculation with tumor. Injections of filtrate were also continued afterward until tumor tissue was removed for transfer to F₁ and F₂. Three rabbits of the latter group (numbers 214, 215 and 216) were likewise given prophylactic injections of the filtrate. Injections following inoculation with tumor were continued to date.

SUMMARY

The sterile filtrate of *B. histolyticus* growing on the Brown-Pearce rabbit epithelioma was injected under a variety of experimental conditions into rabbits having the same type of tumor from which the filtrate was prepared. Injections of this filtrate were found to have no apparent effect on the rate of growth of the tumor or on the microscopic appearance of the tissue. Even when the tumor was propagated through two generations of hosts, both of which had received injections of the bacterial filtrate before and after inoculation with the tumor, is highly malignant potentialities were not checked.

TABLE 6.—*General Summary of the Preceding Tables.**

No takes		Tumor Growth Static or Regressive		Tumor Growth Progressive		Died of Tumor Metastases	
Treated	Non- treated	Treated	Non- treated	Treated	Non- treated	Treated	Non- treated
76	82	80	87	90	97	74	75
215	211	89	96	13	201	77	73
...	...	206	210	205	208	78	91
...	...	...	...	214	209	79	92
...	...	...	...	216	212	81	95
...	...	...	...	...	217	88	202
...	...	...	...	...	...	93	204
...	...	...	...	...	...	94	213
...	...	...	...	...	...	98	...
...	...	...	...	...	...	100	...
...	...	...	...	...	...	19	...
...	...	...	...	...	...	12	...
...	...	...	...	...	...	207	...
...	...	...	...	...	...	15	...

*The figures represent the identification numbers of the rabbits.

4. Note Re Goldfeder.

Appellees' Exhibit 1E.

A Study of the Effect of "Anti-Cancer Preparations" on Malignant Tissues Grown in Vitro and in Vivo, A. Goldfeder. Am. J. Cancer 33:560-567, 1938.

Goldfeder studied the effects of the Schmidt vaccine, ensol. and Jacobs' hormone extract on malignant tumor tissue grown *in vitro* and *in vivo*. No inhibitory effects were obtained with any of these preparations. Photomicrographs of the tissue cultures are included.

5. Paper by G. H. Ettinger, B.A., M.D.

From Appellant's Exhibit 3.

413 *Effects of Ensol on Transplantable Mouse Tumour*

Department of Physiology, Queen's University

Following the publication of his paper "The Study and Treatment of Cancer by Proteolytic Enzymes" (1935) Dr. H. C. Connell asked me, in October, 1935, to test the effect of an ensol, made from mouse tumour, on the growth *in vivo* of that tumour. Gye, in the meantime, reported (1935) that ensol treatment had no effect on the growth of experimental mouse tumour in his laboratory.

All experiments were done on mouse carcinoma "63". These tumours are usually well developed in 2 to 3 weeks after transplantation. Normal growth is rapid; a young tumour may double or treble its volume in a week. The tumours tend to break down spontaneously in the core in about 3 to 4 weeks, but the margin grows and may continue to grow for 3 to 4 months after necrosis has started. Ulceration is common 3 to 5 weeks after transplantation, and may be followed by discharge of some necrotic material; the medial margin, however, continues to grow. Metastases are rare. Untreated tumours

414

usually kill within 15 weeks. Regression sometimes occurs spontaneously. With the strain of tumour used in these experiments regression occurred in 7 of 144 control mice.

All transplants do not grow. This may be due to poor seed, infection at transplantation, or individual natural resistance. Very often an animal which resist growth of the first graft shows resistance to later transplants.

The transplantable type of cancer is widely used for investigation, but is open to the objection that it may not conform to life processes of human cancer, since the latter is invariably spontaneous and not judged transplantable. For this reason spontaneous tumors in mice are believed by some investigators to be better for testing the action of carcinolytic agents.

During these experiments the tumours were measured weekly or semi-weekly with calipers. The effect of any treatment on experimental tumour growth may be measured by (a) delay in onset of growth, (b) length of survival of tumour-bearing animals and (c) regression of the tumour. In successful treatment of human patients with ensol, Dr. Connell reported early and fairly rapid regression of the tumour mass. In experiments on mouse tumours, then, if the tumour manifested continued growth under treatment, it was assumed that the treatment had failed to cause regression.

Three types of experiment were done:—

(a) Effects of repeated subcutaneous injections of ensol on the growth of well-established (2-3 weeks old) tumours.

(b) Attempts to suppress the growth of transplants by repeated subcutaneous injections of ensol immediately after transplantation.

(c) Attempts to immunize mice against the growth of transplants by repeated injection of ensol before transplantation.

All ensol used was made under Dr. Connell's supervision in his laboratory, from healthy mouse carcinoma "63" according to the formula given in his paper (1935). Injections were made under the skin, away from the tumour

mass. The doses used were either 0.25 c.c. of a 1/100 dilution in normal saline, or 0.25 c.c. of undiluted ensol. Calculated on the basis of the human dose of 2 c.c. for a 150 lb. man, these doses for a 25 gramme mouse would be from $3\frac{1}{3}$ to 340 times those given to human patients.

415 In experiments under (b) and (c) it was assumed that, if the transplants grew progressively for 4 weeks after treatment with ensol was started, the treatment had failed to prevent or restrain the growth. Nevertheless, in certain of the experiments the animals were observed until their death.

I. Effect of Ensol on Growing Tumours

Experiment I

35 mice transplanted. 3 weeks later, 16 mice given ensol treatment; 19 mice left for control. Treatment consisted of subcutaneous injections of 0.25 c.c. ensol solution diluted 1/100 with sterile normal saline. Treatment continued for 2 weeks. Growth of tumour was observed periodically until death.

Results

Rapid growth of tumour in 13 treated, — 15 controls

Moderate “ “ “ “ 3 “ — 4 “

Regressions “ “ “ 0 “ — 1 “

Survival of mice after start of treatment:—

Less than 9 weeks 9 treated, — 8 controls

9 weeks or longer 7 “ — 10 “

Experiment II

30 mice transplanted; 2 weeks later 12 mice given ensol treatment, 18 left for control. Treatment consisted of subcutaneous injections of undiluted ensol, 0.25 c.c. given daily for 2-3 weeks. Growth of tumour was observed for 4-6 weeks after transplantation, when animals were killed and tumours examined.

Results

Progressive growth of tumour..	12 treated	—	17 controls
Regression of tumour.....	0	“	— 1 “
Died within 6 weeks	2	“	— 1 “

All other mice had actively growing tumours when killed.

II. Effect of Ensol Injected Immediately after Transplantation

Experiment III

47 mice used, 20 for treatment, 27 for control. Ensol mice given ensol 0.25 c.c. diluted 1/100 with sterile normal saline, for 3 days, transplanted on 3rd day, then given ensol for 4 more days. Control mice transplanted the same day as the treated mice. Growth of tumour was observed until death.

Results

Active growth in.....	18 treated mice	—	26 control mice
Regressions in	1 “ mouse	—	1 “ mouse
No growth of graft in.	1 “ “	—	0 “ “

416 Survival of cancerous mice after start of treatment:—

Less than 9 weeks	12 treated mice	—	16 controls
9 weeks or longer	6 “ “	—	10 “

Onset of growth of transplants was not delayed in treated mice.

Experiment IV

23 mice transplanted; 11 used for treatment, 12 for control. Treated mice given undiluted ensol 0.25 c.c. daily for 3 weeks, starting 2 days after transplantation. Growth of tumor observed for 4-6 weeks when mice were killed and tumours examined.

Results

Active and progressive

growth in	8	treated	mice	—	7	controls
Regressions in	0	“	“	—	0	“
No growth of graft in	3	“	“	—	5	“
Died within 6 weeks	0	“	“	—	0	“

Tumours in other animals were actively growing when mice were killed. Onset of growth of transplants not delayed in treated mice.

III. Effect of Repeated Injection of Ensol before Transplantation

Experiment V

51 mice used; 24 for treatment, 27 for control. Before transplantation the treated mice were given 7 daily subcutaneous injections of 0.25 c.c. ensol solution, diluted 1/100 with normal saline. On the 8th day the treated and control animals were transplanted. Growth of tumours was observed until death.

Results

Progressive growth in	18	treated	mice	—	20	controls
Regressions in	3	“	“	—	4	“
No growth of graft in	3	“	“	—	3	“

Survival of cancerous mice after transplantation:—

Less than 9 weeks	7	treated	—	9	controls
9 weeks or longer	11	“	—	11	“

Onset of growth of transplants was not delayed in treated mice.

Experiment VI

68 mice used; 27 for treatment, 41 for control. Before transplantation the treated mice were given daily injections of 0.25 c.c. undiluted ensol for 8 days (22 mice) or 16

days (5 mice). These and the controls were transplanted the day the last ensol treatment was given. Growth of tumour was observed for 4 to 6 weeks after transplantation.

Results

Progressive growth in	23	treated mice	—	26	controls
Regressions in	0	“	“	—	0
No growth of graft in	4	“	“	—	15
Death within 6 weeks	2	“	“	—	0

Tumours in other mice were actively growing when killed. Onset of growth of transplants was not delayed in treated mice.

417

Conclusion

Ensol made from mouse carcinoma “63” does not check the growth of transplants of “63” in mice if given subcutaneously prior to transplantation, immediately after transplantation, or after the tumour growth has become well established.

The expenses of this research were defrayed by the Hendry Connell Research Foundation.

References

Connell, H. C., “Study and Treatment of Cancer by Proteolytic Enzymes.” Can. Med. Assoc. Jour., 1935, 33, 364.

Gye, W. E. “Treatment of Cancer by Proteolytic Enzymes”, Br. Med. Jour. 1935, II, 760.

Action of Activated Ensol on Transplantable Mouse Tumour

G. H. Ettinger, B.A., M.D.

Department of Physiology, Queen's University

It was reported from the Ensol Clinic that ensol, activated with cysteine, gave satisfactory results in those patients who had previously been refractory to treatment. In view

of the unsuccessful results in treating tumours in mice with mouse ensol, it was decided to test the effect of activated ensol on "63" carcinoma.

Experiment

36 mice were transplanted. 5 days later 16 mice were given treatment with activated ensol; 20 mice retained for control. Treatment consisted of subcutaneous injection of 0.35 c.c. activated ensol which was diluted in proportion of 1.5/1 in process of activation. The ensol was activated daily with cysteine in Dr. Connell's laboratory, 1 hour before injection. Injections were repeated daily for two weeks. Growth of tumour was observed periodically for 5 weeks.

Results

Active and progressive

growth in	8	treated mice	—	6	controls
Delayed growth in	2	" "	—	3	" "
Regressions in	1	" "	—	1	" "
No growth of graft in	5	" "	—	10	" "

Conclusion

Growth of "63" mouse carcinoma is not delayed nor suppressed by treatment with mouse ensol activated with cysteine.

The expenses of this research were defrayed by the Hendry Connell Research Foundation.

418 *Action of Human Ensol on Mouse Carcinoma "63"*

G. H. Ettinger, B.A., M.D.

Department of Physiology, Queen's University

Clinical results with human ensol indicated carcinolytic effects which were not paralled by treatment of mouse carcinoma with mouse ensol. It was thought that human ensol

might contain a principle which was missing in mouse ensol, but might not be species specific.

Experiment

72 mice were transplanted with "63" mouse tumour. 33 were used for treatment, 39 retained for control. Treated mice were given subcutaneous injections of human ensol, diluted 1/10 with normal saline, 0.5 c.c. daily for 3 weeks, starting 2-5 days after transplantation. Growth of tumours was observed for 5-6 weeks after transplantation.

Results

Active and progressive

of tumour, ...	20	treated	—	28	controls
Delayed growth	4	"	—	3	"
Regression of tumour	0	"	—	0	"
No growth of graft	9	"	—	8	"
Death within 6 weeks	6	"	—	12	"

Conclusion

Human ensol exerts a slight restraint of growth on "63" mouse tumour *in vivo*.

These experiments should be repeated, if this conclusion is to be established.

The expenses of this research were defrayed by the Hendry Connell Research Foundation.

Action of Ensol on the Dog-Heart

G. H. Ettinger, B.A., M.D.

Department of Physiology, Queen's University

The use of ensol in the treatment of carcinoma was based on the hypothesis that *B. histolyticus*, growing on a substrate consisting chiefly of cancer cells, produced an enzyme capable of specifically destroying carcinoma. According to such an hypothesis, an ensol made using heart-

muscle as a substrate should be capable of destroying the heart *in vivo*.

This problem was attempted on one dog. Dog-heart ensol was made in Dr. Connell's laboratory, from two
419 separate specimen's (September 6, 1935, and November 13, 1935). A healthy dog was selected for injection of this ensol. Its blood-pressure and electrocardiogram were recorded, and heart-sounds observed. Ensol was then given, 1 c.c. subcutaneously, daily, for 14 weeks. The animal was then examined as before. No damage to the heart's action was detected. One month later the animal was killed. The heart was of normal size and colour. Histological sections showed no degenerative change in the myocardium.

CONCLUSION

Heart ensol, injected daily into the dog for 14 weeks, creates no detectable functional or organic damage. It is concluded that it is not capable of specifically attacking heart-muscle.

The expenses of this research were defrayed by the Hendry Connell Research Foundation.

TOXIN PRODUCTION IN MANUFACTURE OF ENSOL

G. H. ETTINGER, B.A., M.D.

Department of Physiology, Queen's University

In an experiment in which ensol, prepared by the growth of *B. histolyticus* on dog-heart, was administered to a healthy dog daily for a period of six weeks, the heart of the animal does not appear to have been damaged. This is explained by Holsgrove and Connell on the hypothesis that the specific enzyme in heart-ensol is toxic, and so stimulates the production of an antitoxin which prevents enzymic destruction of the heart muscle *in vivo*, as well as neutralizing the direct toxic effects.

This hypothesis is based on their observation that *B. histolyticus* grown on a brain medium produces a large amount of toxin, and grown on Robertson's meat medium, little if any. Holsgrove and Connell suggest that under conditions in which the substrate provides readily assimilable food, no toxin is produced, but when the cells containing this food require attack before yielding it up, the organisms yield a toxin, bound up with the enzyme, which is essential for the release of this food material. According to these investigators then, *B. histolyticus* grows readily on human cancer cells *in vitro*, yielding a specific enzyme which has no toxin bound up with it. For this reason the ensol may be administered to a cancer patient without toxic effects, so without antitoxin production, and so promote dissolution of the cancer in the patient indefinitely.

420 They suggest that an attempt be made to demonstrate the production of a toxin in these ensols which, produced by the growth of *B. histolyticus* on certain animal cells *in vitro*, fail to produce destruction of that tissue when introduced in small quantities in the living body of the animal. They also wish to demonstrate that ensol grown on cancer tissue produces no toxin, and to explain in this way the success of its administration.

In order to get information on this point it was suggested that ensol be made from a naturally occurring parasitic type of cell, viz., the chorionic epithelium, and that this be injected into the body of a pregnant animal. The chorionic epithelium resembles the cancer cell in many aspects of its growth, and, as well, may take on malignant characteristics. If injection of this ensol caused abortion it would, on the hypothesis of Holsgrove and Connell, be taken as evidence of *want* of toxic properties, for it would be judged to have caused free destruction of the placental epithelium in the way that human ensol destroys cancer, without the production of antibodies.

An investigation of this kind will be long and troublesome. It should not be attempted *for this purpose* until it has been demonstrated that in the animal under investigation cancer responds to cancer ensol. Otherwise it might be taken to demonstrate (assuming that abortion occurs) that placental ensol is toxic. It might, of course, be worth doing for the purpose of investigating the specificity of placental ensol.

I am not satisfied, however, that it has been proven that cancer ensol does not contain toxin. The existence of toxin in filtrates from cultures of histolyticus is described in text books on bacteriology. This toxin is produced quickly, is destroyed quickly, and may be removed by process which involved prolonged filtration. Toxin produced by growth on cancer cells might therefore have been destroyed or removed from the material which I introduced into mice some time ago. The fact that patients experience no toxic effects may be due to the small doses given.

I suggest that I be permitted to test on mice the toxic effects of human cancer ensol, made by growth of histolyticus for no longer than 24 hours, and filtered rapidly, so that optimum conditions for toxin production be employed.

* * * * *

IV. DISPOSITION OF CASE BY DISTRICT COURT.

A. Findings of Fact and Conclusions of Law.

158 Endorsed: Filed Feb 25 1941 Charles E. Stewart, Clerk

In the District Court of the United States for the
District of Columbia.

Civil Action, No. 4819.

CANADIAN-AMERICAN PHARMACEUTICAL COMPANY, *Plaintiff*,

v.

CONWAY P. COE, COMMISSIONER OF PATENTS, *Defendant*.

A. Findings of Fact.

1. This is a suit brought under the provisions of Section 4915 R. S. (U. S. C., title 35, sec. 63) in which it was sought to have the court find that the plaintiff Canadian-American Pharmaceutical Company is entitled to the issuance of a patent on the application of Hendry C. Connell, Serial No. 137,931, filed April 20, 1937, relating to Pain-Alleviating Material and containing claims 2, 3, 4, 6, 7, 8, 9, 10, 11 and 12, as set forth in paragraph 8 of the complaint.

2. The Connell application in issue discloses a process for producing a substance allegedly capable of reducing the pain resulting from cancer which consists in growing B. Histolyticus on cancer tissue for such a length of time that the cancer tissue is almost completely destroyed and separating the liquid from the solid portion of the resulting incubated mass. The application also relates to the product obtained by such process.

159 3. The prior art does not disclose or anticipate either the process or the product.

4. There is no evidence that plaintiff's product causes any harmful effects.

5. That while the testimony of plaintiff's witnesses and certain of the exhibits are to the effect that the invention

has reduced pain due to cancer in approximately 65% of the cancer patients treated therewith, this evidence when considered in connection with the negative tests reported by Gye, Pommerenke, Goldfeder, and Rusch & Preston in various publications of the American Journal of Cancer, the Journal of the American Medical Association, and the Proceedings of the Society of Experimental Biology and Medicine, fails to establish that the invention is sufficiently reliable, useful and important to warrant the grant of a patent.

B. Conclusions of Law.

1. The subject matter of the claims in issue is not possessed of sufficient utility to justify the issuance of a patent under Section 4893 R. S. (U. S. C., title 35, sec. 36).

2. Plaintiff is not entitled to a patent containing claims 2, 3, 4, 6, 7, 8, 9, 10, 11 and 12.

3. The complaint should be dismissed.

DANIEL W. O'DONOGHUE

Feb. 25th 1941

Justice.

B. Judgment.

This cause having come on to be heard and having been tried in open court and argued by counsel for the respective parties upon the pleadings and proofs adduced and submitted to the Court,

It is Adjudged this 25th day of February, 1941, that the complaint in this case be, and the same hereby is dismissed with costs against the plaintiff.

DANIEL W. O'DONOGHUE,

Justice.

V. NOTICE OF APPEAL AND STATEMENT OF POINTS.*Notice of Appeal.*

Notice is hereby given this 20th day of March, 1941, that Canadian-American Pharmaceutical Company, plaintiff in the above entitled action, hereby appeals to the United States Court of Appeals for the District of Columbia from the judgment of this Court entered on the 25th day of February, 1941, in favor of Conway P. Coe, the Commissioner of Patents, against the said Canadian-American Pharmaceutical Company.

ARTHUR G. CONNOLLY
Wilmington, Delaware

JAMES P. BURNS
807 Munsey Bldg.
Washington, D. C.
*Attorneys for Canadian-American
Pharmaceutical Company*

Service of Notice of Appeal and Accompanying Points of Appeal Acknowledged.

W. W. COCHRAN
For the Commissioner of Patents.

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Statement of Points

Now comes the plaintiff, Canadian-American Pharmaceutical Company, by its attorneys, and presents and specifies the following statement of points herein:

That the District Court erred:

1. In not holding that the invention defined by claims 2, 3, 4, 6, 7, 8, 9, 10, 11, and 12 of United States patent application Serial No. 137,931 is sufficiently useful and important to warrant the grant of a patent thereon;
2. In not holding that the articles by Guy, Pommerenke, Goldfeder, and Rusch & Preston were irrelevant to a determination of the issue of utility;

3. In not holding that the testimony of plaintiff's witnesses proved that the invention in issue was sufficiently useful and important to warrant the grant of a patent thereon;

4. In not holding that plaintiff's exhibits proved that the invention in issue was sufficiently useful and important to warrant the grant of a patent thereon;

5. In holding that the subject matter of the claims in issue is not possessed of sufficient utility to justify the issuance of a patent under Section 4893 R.S. (U.S.C., title 35, sec. 36).

163 6. In holding that plaintiff is not entitled to a patent containing claims 2, 3, 4, 6, 7, 8, 9, 10, 11, and 12;

7. In entering judgment in favor of the defendant and dismissing the complaint herein.

Wherefore, the plaintiff prays that the judgment entered herein on the 25th day of February, 1941, be vacated and that a decree be entered adjudging that the plaintiff is entitled to have claims 2, 3, 4, 6, 7, 8, 9, 10, 11, and 12, inclusive, allowed in said application Serial No. 137,931, and authorizing said defendant to issue to the plaintiff a patent on said application containing said claims on the filing in the Patent Office of a copy of the Court's adjudication and otherwise complying with the requirements of law; and for such other and further relief as the case may require and to the Court may seem meet. •

JAMES P. BURNS

ARTHUR G. CONNOLLY

*Attorneys for Canadian-American
Pharmaceutical Company*

Dated, Washington, D. C.

March 20, 1941

FILED SEP - 5 1941

Joseph R. Starnes

**In the United States Court of Appeals
for the District of Columbia**

APPEAL NO. 7893

CANADIAN-AMERICAN PHARMACEUTICAL COMPANY, APPELLANT

v.

CONWAY P. COE, COMMISSIONER OF PATENTS, APPELLEE.

APPEAL FROM THE JUDGMENT OF THE DISTRICT COURT OF THE
UNITED STATES FOR THE DISTRICT OF COLUMBIA

BRIEF FOR APPELLEE

W. W. COCHRAN,
*Solicitor, United States Patent Office,
Attorney for Appellee.*

H. S. MACKEY,
Of Counsel.

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In the United States Court of Appeals for the District of Columbia

NO. 7893

CANADIAN-AMERICAN PHARMACEUTICAL COMPANY, APPELLANT

v.

CONWAY P. COE, COMMISSIONER OF PATENTS, APPELLEE

BRIEF FOR THE COMMISSIONER OF PATENTS

INTRODUCTION

This is an appeal from the judgment of the District Court of the United States for the District of Columbia (App. 180) in an action brought by the appellant under Section 4915 R. S. (U. S. C., title 35, sec. 63), to authorize the Commissioner of Patents to issue to appellant a patent on the application of Hendry C. Connell, Serial No. 137,931 entitled New Pain-Alleviating Material.

APPELLANT'S DISCLOSURE

Appellant's application relates to a process and product for an alleged pain alleviating material for use in cases of cancer. In the process, cancer tissue is inoculated with a proteolytic micro-organism and this material is grown for a sufficient period of time at least partially to decompose the cancer tissue. The liquid is then separated from the solid portion and sterilized. The liquid so produced is the alleged pain alleviating material and has been given the name "Ensol" by appellant.

The question involved herein is solely one of utility of the product. In appellant's statement of the case (Brief 2) it is

to be noted that appellant states on the question of utility: "The District Court has found as a fact that the testimony of plaintiff's witnesses and certain of the exhibits was to the effect that the invention had reduced pain due to cancer in approximately 65 percent of the cancer patients treated therewith." While this statement is true as far as it goes, it is but a partial quotation of the finding of the Court and raises the inference that the Court found as a fact that the product had utility in 65 percent of the cases. It is to be noted that the complete finding of fact states:

That while the testimony of plaintiff's witnesses and certain of the exhibits are to the effect that the invention has reduced pain due to cancer in approximately 65% of the cancer patients treated therewith, this evidence when considered in connection with the negative tests reported by Gye, Pommerenke, Goldfeder, and Rusch & Preston in various publications of the American Journal of Cancer, the Journal of the American Medical Association, and the Proceedings of the Society of Experimental Biology and Medicine, fails to establish that the invention is sufficiently reliable, useful, and important to warrant the grant of a patent.

(App. 179.)

It therefore appears appears that the Court's finding is not one of utility in 65% of the cases as might be inferred from appellant's partial quotation but is, in fact, a finding of no utility when considering all the evidence adduced before the Court.

SUMMARY OF ARGUMENT

1. The utility required to justify issuance of a patent on products such as those involved herein must be established by convincing proof.

2. The testimony fails to establish the necessary degree of utility to warrant the issuance of a patent. The testimony for the most part is that of interested parties or is based on a study of case histories prepared by interested parties.

3. The documentary evidence introduced by appellant fails to establish the utility of the product. Most of the documentary exhibits are publications of the Hendry Connell Foundation and are self-serving declarations which are of little aid in establishing utility. The case histories reported in most of

the publications are fragmentary and so bound up with other considerations as to be of little value in establishing the utility of the product as a pain alleviator.

4. The publications which are the result of the work of independent experts negative the utility of the product. These publications, although written as a result of tests upon animals, reveal that the use of "Ensol" results in no symptomatic improvement and are therefore clearly indicative of the absence of any material relief of pain or other symptoms.

5. The need of a medical practitioner for a product that reduces pain in cancer cases is entirely irrelevant to the question of the utility of "Ensol" for that purpose.

6. The grant of a patent is regarded as an approval by a governmental agency of the utility of the product set forth therein. The ability to mark a product as patented has an effect on the salability of that product in the minds of many practitioners as well as laymen and in this respect the patent is regarded as a stamp of approval by the government.

ARGUMENT

1. Utility must be established by convincing proof

The subject matter of the present case relates to a medicinal product purportedly for relieving pain in cancer cases as indicated above. It is submitted that in such cases public policy demands that utility be established by convincing proof. Certainly the public interest is not served by the indiscriminate patenting of medicinal preparations of little or no utility. While in mechanical cases there is a justification for a holding of utility even where the device is crude and imperfect since it points the way to advance and skilled craftsmen can in most cases improve and perfect the device, there is no such justification in the case of medicinal preparations. In the case of medicinal preparations the public is led to believe by the very act of patenting that a product is efficacious for the purposes for which it is sold, whereas, in reality, the product may be wholly lacking in utility if not actually harmful.

A search of the recorded cases reveals few having to do with the question of utility in relation to medicinal preparations

and products of like nature, but such few as there are appear uniform in requiring convincing proof of utility. In the case of *Hall v. Duart Sales Company, Ltd. et al.*, 28 F. Supp. 838, decided by the District Court for the Northern District of Illinois, the subject matter involved constituted a skin cream having a milk base. In this case, although there was strong argument as to the utility of milk as a skin whitener, including reference to the famed Cleopatra baths which the Court branded as a myth, the Court nevertheless held the product invalid as lacking in utility. In the case of *Hoover et al. v. Eckerds Cut Rate Medicine Company*, 63 F. (2d) 813, the Third Circuit Court of Appeals held that a dentifrice which purported to calcify the teeth was lacking in utility. This holding was made in spite of tests which purported to support the contention of utility. The Court held that the porosity of the teeth, the existence of which is necessary to support plaintiff's theory of artificial calification of the teeth is in the realm of debatable theory and consequently utility had not been established. Again in the case of *In re Oberweger*, 115 F. (2d) 826, the Court of Customs and Patent Appeals had before it the question of utility of a preparation for growing hair. In this case the Court held:

It was the view of the tribunals below that the affidavits were weak in character and were not sufficient to show utility for a concoction which belongs to a class of compositions which from common knowledge has long been the subject matter of much humbug and fraud.

The Court after discussing the case of *In re Perrigo*, 48 F. (2d) 963, had this to say in addition.

Very much like the situation at bar, the affidavits in that case did not afford *convincing proof of utility*. Certainly there is nothing in this record to show that appellant's composition is any better than the many hundreds of similar concoctions that have been advertised and sold to a credulous public since the beginning of recorded history. It is a matter of common knowledge that numerous preparations, similar in many respects to the one at bar, have been advertised and sold, for the purpose of

producing hair on bald heads and which were totally lacking in utility, often harmful to the human body, and whose sale was generally understood to be a fraud upon the public.

Having in mind the *particular subject matter involved* in the instant alleged invention, we are in full agreement with the tribunals of the Patent Office that the claims which are before us on their merits were properly rejected for lack of patentable utility. [Emphasis added.]

From these cases it appears that the Courts have held wherever the question was before them that in the case of medicinal preparations there must be convincing proof of the utility of the product. The case at bar is closely parallel to that of *In re Oberweger, supra*, since it is a matter of common knowledge that cancer cures and preparations for the alleged relieving of pain in cancer cases have often been advertised and sold to a credulous public just as have numerous concoctions for growing hair upon bald heads.

It is submitted that the cases cited by appellant in its brief, page 12, to support its contention that utility is established even though an article be crude and imperfect are irrelevant to the present case. These cases all relate to mechanical devices ranging from machines for pulling candy to reaping machinery. The subject matter involved herein is not a machine but a medicinal product and a crude and imperfect medicinal product is often more harmful to the public than no product at all. It is submitted, therefore, that in this class of cases clear, unequivocal and convincing proof of utility should be present in order to warrant the issuance of a patent.

2. The testimony fails to establish the necessary degree of utility

The testimony adduced in the instant case appears to be characterized by a certain unscientific enthusiasm which leaves its credibility open to question. This unscientific approach and readiness to accept something new as established is particularly well exemplified by the history of the development of this product. Doctor Hendry C. Connell, the inventor, is an

eye, ear, nose, and throat specialist (App. 30) and it appears that he was originally interested in, and was working on a product which he hoped would dissolve cataracts. It occurred to him during this work that possibly he could use such a process on other foreign protein substances of the human body. This led him to procure some cancer tissue and grow organisms thereon and he noted that the cancer tissue disintegrated very rapidly. Without much further ado or tests to any great extent, as indicated by the record, he inoculated a Chinese patient who was suffering from cancer of the eyeball. Connell states, "I decided that it would do the Chinaman no harm at least—at least I did not think it would—and I tried it." (App. 32.) Subsequently to this first use it was used on other patients and sent to physicians all over the world with apparently very little experimentation on animals such as would ordinarily be considered to be the proper scientific approach.

By interrogatories, Doctor James Cameron Connell, father of Hendry C. Connell, also testified to the utility of the product. Although it is to be noted that James Connell testifies that he was interested in the study of cancer for fifty years or more (App. 12) it does not appear that he is a cancer specialist. As a matter of fact Hendry C. Connell testifies that his father was a well-known eye, ear, nose, and throat specialist (App. 30) and therefore it is submitted that this testimony, insofar as it relates to opinion on the treatment of cancer and pain alleviations in such cases, is of little weight.

In addition to the testimony of Hendry Connell and his father, there has been submitted testimony of Walter Thomas Connell (no relation to the inventor) and E. P. Johns who were appointed by the Canadian Government to study the use of Ensol in the treatment of cancer cases. It is apparent from the testimony of these two men that their investigation had covered a period of little more than a year, an exceedingly short time for scientific investigations such as we are here concerned with. Furthermore it is to be noted that much of this study and investigation constituted a review of records and a study of case histories which were available at the Hendry-Connell Foundation. Since these case histories and records were prepared for the most part by the parties involved herein, testimony

which is based on the study of these records adds little to the interested testimony previously adduced. Johns in stating his conclusions as to the efficacy of "Ensol" in the treatment of cancer states that he had examined the records and some cases personally and at the same time recognizes the reports of others whose work indicated negative results. He, however, states, "Personally, we prefer to believe the evidence which was given by a large number of investigators on a large series of cases rather than the evidence presented by four investigators on a comparatively small series of animals." (App. 68.) It is submitted that such testimony indicates an unscientific ignoring of evidence which is adverse to that which it is desired to believe and it is such an unscientific approach which characterizes the testimony adduced on behalf of the appellant which, it is submitted, fails to establish the utility of the product. In addition to these witnesses, Robert Norman Erwin also testified relative to the utility of appellant's product. He, however, has handled a very small number of cases and his study does not appear to have been sufficiently extensive to constitute a basis for holding the product useful.

3. The documentary evidence introduced by appellant fails to establish utility

The documentary evidence introduced by appellant is, for the most part, from bulletins prepared by the Hendry-Connell Foundation and is therefore self-serving and of little value. Most of the cases reported in these various documents are exceedingly fragmentary and in some part do not deal with the question of pain but deal with the question of regression of the tumor and other factors. Even where pain is considered it is in a large measure bound up with other factors and other treatments. Likewise the accuracy of reporting in some of these cases appears open to question. This is apparent from a study of the various reports on the Chinese patient, one S. L. In the first report appearing at page 86 of the Appendix there is the statement, "The pain had eased completely." However, as this patient died six months after his first treatment there is the report of the post mortem performed appearing at pages 89 to 91 of the Appendix. In the comment on this case by H. C. C.

(presumably Hendry C. Connell, the inventor) this statement is found:

It is evident that I was quite justified in the experimental use of a new biological product in this case. There was no harmful reaction, there was a recession of the orbital tumour and *some mitigation of pain.*" [Emphasis added.]

It therefore appears that in two different reports on the same case, one report states that the pain had eased completely whereas the second report merely states that there was some mitigation of pain, a quite different observation. This contradiction, of its very nature, raises the question of the accuracy of other like reports and case histories wherein there is a report of cessation or easement of pain. Furthermore, many of the reports are very fragmentary and are characterized by the statement, "No termination report." Since it appears from the testimony that in untreated cases a tumor sometimes regresses for a while (App. 76) and since regression or lessing of the growth eased pain (App. 60) it would appear that there would be some cases where pain would be eased or cease for a while and then increase whether treated or not. Consequently, reports which are merely fragmentary and indicate easing or cessation of pain at one period would appear to have no merit in determining the utility of a product such as here in question.

4. Independent studies negative utility

The studies of independent experts introduced by appellee through the medium of the publications of Gye, Rusch & Preston, Pommerenke and Goldfeder with which must be considered the work of Ettinger as reported in appellee's Exhibit 3, clearly indicate that no useful results are obtained by the use of the product in question. Gye in his report states that the growth of a tumor had not been checked or affected in any way by treatment with Ensol (App. 148). Rusch & Preston carried on extensive tests using mice as test animals. Their conclusions (App. 153) are that the solutions prepared according to the method of Connell were without any effect in prolonging the life of the animals, in preventing or decreasing the number of metastases or in inhibiting the rate of tumor growth. Like-

wise Pommerenke who carried on tests on rabbits concluded (App. 164) that no difference could be observed in the growth habit of the tumor in treated and nontreated animals, and again, at App. 167, that injections of Ensol had no apparent affect on the rate of growth of the tumor or on the microscopic appearance of the tissue. Goldfeder's conclusions were to the same effect, namely, that no inhibitory effects were obtained (App. 168). Ettinger, as is apparent from the report (App. 168 to 178), made extensive tests on mice. His tests indicate that mouse carcinoma is not delayed or suppressed by treatment with mouse Ensol. He did find (App. 165) that human Ensol exerts a slight restraint on the growth of mouse tumor. He, however, states that these experiments should be repeated if this conclusion is to be established and it would seem from a consideration of this test that such repetitions should certainly be made before any conclusion could be arrived at since the only element which would appear to support any contention that human Ensol exerted a restraint on the growth of mouse tumor would appear to reside in the fact that tumor was delayed in four cases of treated mice, whereas it was delayed in only three cases of untreated mice. Certainly such a slight variation does not appear to be one upon which a scientific conclusion could be based. It would appear rather to indicate no effect rather than utility of Ensol. It is further to be noted that Ettinger in the study of toxic properties of Ensol is not satisfied that such toxic properties are not present (App. 168). This is in contradiction to the testimony of Johns who states that he is satisfied that Ensol is harmless and contains no toxin. This statement was apparently made after the inoculation of Ensol into a group of 70 entirely normal patients extending over a period of 20 to 30 inoculations without having those patients experience any deleterious effects. This appears to be another instance of a somewhat unscientific approach. Certainly this relatively small number of tests on healthy patients would not appear to be a sufficient basis for the categorical statement that the product was harmless when used extensively on patients suffering from cancer.

The appellants have argued strongly that the articles of Rusch & Preston, Pommerenke, Gye, and Goldfeder are of no

value and this argument appears to be based on various reasons which are set forth extensively in the testimony of James C. Connell (App. 26 and 27) which it is believed might be well considered in detail. It is stated first that the work of these experimenters did not deal with pain relief since animal experimentation does not indicate whether pain was being relieved or not. This is true, but inasmuch as all the case histories are so interbound not only with pain relief but also with recession of the tumor, change in tumor growth, and other symptomatic improvements, it is submitted that other work which reveals that such symptomatic improvements and change and recession of the tumor growth are not present is directly contradictory to the testimony adduced by appellant and clearly indicates the lack of utility of the product. Furthermore, it must be noted that although it is stated that the sole claim for the product is as a pain alleviator and "anything else that goes with it" (App. 52) this product has been used where pain was not even a symptom (App. 50). Therefore, it would appear that work of independent experts which reveals no symptomatic improvement or, in fact, change in any respect, clearly indicates lack of utility. In this respect it is also to be noted that the work of these independent experts was based on a scientific foundation of the use of treated and untreated subjects whereas the testimony in cases used to support appellant's allegation of utility is based merely on a series of treated cases wherein every symptomatic improvement regardless of its cause is accredited to Ensol. James Connell further states that the work of these independent experts was carried on independently of the inventor although they were invited to visit his laboratory. It is not seen how this independent work could mitigate against the validity of their conclusions. Rather it would be expected that true scientific approach would recommend entirely independent investigations. James Connell further states that there is no evidence that the product employed by these men was similar to the product in question. This statement does not appear to be borne out by the facts. Rusch & Preston and Pommerenke set forth with great particularity the manner in which they prepared the product and this corresponds in every

respect to the process set forth by Connell in his patent application. Certainly men, experts in this field, could prepare the product from these teachings which it is apparent that they did. Furthermore, this objection cannot lie against the adverse report by Ettinger who worked in conjunction with the Hendry-Connell Foundation.

It is further contended that the experiments performed by these men were completed within a few weeks and hence their work was superficial and inadequate. It is contended on behalf of appellant that the expected life of these animals would be too short to note improvement. However it is to be noted that the very first case reported by appellant was stated to show improvement in ten days (App. 73). Inasmuch as some of these animals lived for nine weeks or longer, as evidenced by the work of Ettinger (App. 173), it is submitted that adequate time was available. It is further contended that the investigators conducted their experiments on the supposition that the active principle in the solution was an enzyme whereas it is now known to be antigenic in character. The validity of this contention is not apparent. What relation the theory of what does or does not cause the product to produce the results alleged appears to be wholly immaterial. The question of utility is one of fact and bears no relation to the theory which may be proposed to support this fact. The experiments of these independent experts reveal the lack of utility of the product and what theory is advanced to account for supposed reactions would appear to have no bearing on the facts as revealed by the tests. James Connell further testifies (App. 27) that from a scientific point of view negative results published were of no value whatever. This is a categorical statement, the basis of which does not appear to be well founded. It reveals rather the tendency of the witnesses to ignore that which is adverse and to consider only that which they might construe to support their position.

5. The need of a pain alleviator is entirely irrelevant

It is admitted that the need of medical practitioners for a product which would alleviate pain in cases of cancer is great. What bearing this need has upon the question of the utility

of Ensol is not apparent. From these considerations it might as well be argued that because there was great need for a cure for cancer, tuberculosis or many other diseases that therefore the product Ensol was useful for those purposes. It is believed that this great need has made the witnesses and other practitioners over enthusiastic and inclined to accept a new product as being efficacious where, in fact, it was not, and to attribute any improvement from whatever cause derived to the new product. That the need is great is admitted but it is submitted that the product in suit does not supply this need.

6. A patent grant is regarded as an approval of the product by the government

It is recognized that other governmental agencies than the Patent Office are charged with the duty of protecting the public in the case of drugs and other medicinal products. However, rightly or wrongly, the public considers that when a device is patented it has been approved by the government, and the mere patenting of the device has an advertising value in and of itself which leads the public to place reliance thereon and to entertain hopes which may never be fulfilled. It is therefore submitted that in cases of this kind utility should be convincingly shown before a patent is granted. Certainly the progress of science and the useful arts is not promoted by an indiscriminate granting of patents on medicinal preparations of doubtful value.

CONCLUSION

In conclusion it is submitted that utility of the product involved herein, namely Ensol, has not been sufficiently established to warrant the granting of a patent and that the ruling of the lower court should be affirmed.

W. W. COCHRAN,
Solicitor, United States Patent Office,
Attorney for Appellee.

H. S. MACKEY,
Of Counsel.

REPLY BRIEF FOR APPELLANT

IN THE
United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA

No. 7893

CANADIAN-AMERICAN PHARMACEUTICAL COM-
PANY, *Appellant*,

v.

CONWAY P. COE, COMMISSIONER OF PATENTS,
Appellee.

ARTHUR G. CONNOLLY,
JAMES P. BURNS,
Counsel for Plaintiff-Appellant.

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IN THE
United States Court of Appeals

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No. 7893

CANADIAN-AMERICAN PHARMACEUTICAL COM-
PANY, *Appellant*,

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CONWAY P. COE, COMMISSIONER OF PATENTS,
Appellee.

REPLY BRIEF FOR APPELLANT.

INTRODUCTION.*

Defendant concedes on the first page of its brief that the sole question presented is: DOES THE PRODUCT IN ISSUE POSSESS UTILITY? Since this invention is directed to the reduction of pain due to cancer, UTILITY means the ability to accomplish this objective.

Plaintiff has shown that hundreds of patients in the last stages of cancer have experienced a pronounced reduction of pain by the administration of this product. In many of these cases the reduction of pain has been not only complete

* Whenever used in this brief plaintiff designates plaintiff-appellant, defendant designates defendant-appellee, and App. refers to plaintiff's appendix.

but permanent as well. The greater portion of this evidence is based upon the private investigations of physicians throughout Canada and the United States. These physicians had no connection with the inventor or his research organization, and in most instances were personally unknown to him.

In addition to the foregoing, plaintiff has shown that the Ontario Government appointed a group of highly skilled investigators to determine whether this product was beneficial in the treatment of cancer. This group devoted all its time for more than a year to an intensive investigation of this question. As a result of this investigation the Ontario Government approved this product as a harmless and beneficial therapeutic for use in the treatment of cancer. **IT WENT FURTHER, AND PUBLICLY ASSUMED ALL EXPENSES FOR PRODUCING AND SHIPPING THIS PRODUCT THROUGHOUT THE WORLD FOR THE TREATMENT OF CANCER PATIENTS.** More than ten thousand cubic centimeters of this product are being produced each month at the expense of the Ontario Government, for shipment free of charge to physicians throughout the world.

The Ontario Government authorized two of its representatives to attend and testify in this case. These representatives personally engaged in and directed the aforesaid investigation on behalf of the Government. Their testimony is unqualifiedly to the effect that **THIS PRODUCT RELIEVED PAIN IN 65 PER CENT OF THE CANCER PATIENTS TREATED.** (App. 57, 66)

Never in the history of our patent system, so far as plaintiff has been able to determine, has any foreign government officially interceded in support of an invention. The proof in support of utility is so overwhelming, both in character and reliability, that no rational basis exists for a contrary holding. To deny utility is to hold that the Ontario Government is squandering public funds on a worthless product. To so hold is to dispute the integrity

and ability of the official representatives of the Ontario Government and the remaining witnesses below, as well as the hundreds of physicians who independently evaluated and approved this product.

The only evidence relied on by defendant pertains to *animal experiments* for determining the effect of this product on the growth of *transplanted tumors*. These experiments were in no instance directed to, and were of no value in ascertaining pain reduction. (App. 26-28, 58, 67) Even defendant concedes in his brief that his evidence did not deal with pain relief. (p. 10) This concession utterly destroys the flimsy evidence which had been advanced to negative utility. It admits the soundness of the second argument in plaintiff's main brief, namely, that the references relied on to negative utility are irrelevant. It establishes that there was indeed no rational basis for the conclusion reached by the Patent Office tribunals.

Defendant's concession is not lessened by his illogical theory which would determine pain relief, not by tests directed thereto, but rather by a consideration of transplantable animal tumor recession and other criteria quite unrelated to pain. As defendant's evidence is not directed to pain relief it is submitted that the court below was clearly in error in holding that it negated utility.

THE ATTACK ON PLAINTIFF'S WITNESSES.

Defendant states in its brief that—"The testimony adduced in the instant case appears to be characterized by a certain unscientific enthusiasm which leaves its credibility open to question." (p. 5) Following this is an attack on the integrity and ability of each of plaintiff's witnesses.

This attempt to belittle the testimony of the five witnesses who testified in this suit is unwarranted. Each of these witnesses is a well known and respected member of the Canadian medical profession. One of them was president of the Medical Council of Canada and Dean of a leading Canadian Medical School. Two of them were official representatives

of the Ontario Government selected for their widely recognized ability in their chosen fields. One of them was a leading Toronto practitioner. The inventor was a successful practitioner whose research abilities had been publicly acknowledged by the Canadian National Research Council.

That the integrity and ability of these witnesses is free from doubt is clear from the cursory cross-examination to which the defendant subjected them. Although these witnesses testified in detail about their individual investigations of the product in issue and its outstanding utility they received practically no cross-examination from the defendant. Their testimony is complete, consistent, unchallenged and uncontradicted. There is absolutely no basis in the record or in fact to justify defendant's deplorable accusations.

Defendant states that, "Without much further ado or tests to any great extent, as indicated by the record, he (the inventor) inoculated a Chinese patient who was suffering from cancer of the eyeball." (p. 6) If one examines the record, however, one sees that BEFORE TREATING THIS POOR CHINAMAN THE INVENTOR FIRST INJECTED THE PRODUCT IN ISSUE INTO HIS OWN BODY AND MADE CERTAIN THAT IT WAS HARMLESS. (App. 32)

If this was unscientific enthusiasm, as charged by the defendant, then Dr. Connell was willing to risk his life on the value of his product. He preferred to sacrifice his own health before he would jeopardize the health of a destitute Chinaman who at best had only a short time to live. We could use more of this unselfish devotion to the ills of mankind.

Defendant then goes on to state—

"Subsequently to this first use it was used on other patients and sent to physicians all over the world with apparently very little experimentation on animals such as would ordinarily be considered to be the proper scientific approach." (Def. brief p. 6)

As previously mentioned, pain alleviation MUST be determined by treatment of human beings who can describe their sensations. Tests on animals are absolutely valueless for this purpose. Furthermore, the conclusions of hundreds of physicians based on independent investigations are far more important than would be the opinion of the inventor alone. Also, animal tumors are so different from human tumors that it is problematical whether any dependable conclusions whatsoever could be drawn from animal experiments.

The defendant attacks the testimony of Dr. James C. Connell, father of the inventor, as follows:

“Although it is to be noted that James Connell testifies that he was interested in the study of cancer for fifty years or more (App. 12) it does not appear that he is a cancer specialist. As a matter of fact Hendry C. Connell testifies that his father was a well known eye, ear, nose, and throat specialist (App. 30) and therefore it is submitted that this testimony, insofar as it relates to opinion on the treatment of cancer and pain alleviations in such cases, is of little weight.” (Def. brief p. 6)

Dr. James Cameron Connell has had a most illustrious career as is clear from an examination of pages 10 to 12 of plaintiff's appendix. He began actively practicing medicine in 1888. He was on the faculty of Queen's Medical School for almost forty years, for many years of which he was Dean. From 1917 to 1929 he was a member of the Education Committee of the College of Physicians, Ontario and a member of the Educational Committee of the Medical Council of Canada. He was president of the Medical Council of Canada and chairman of the Education Committee.

Defendant is evidently of the belief that eye, ear, nose and throat specialists know nothing about cancer or methods for its treatment. Cancers of the throat are among the most common and difficult to treat. Dr. James Connell has treated many, many cancer patients during his career. Furthermore, any physician who has actually practiced and

taught medicine for more than half a century is eminently qualified to give an opinion on the efficacy of a pain alleviant for cancer cases which he has personally and intimately observed for a period of more than five years.

In the last paragraph on page 6 of its brief, defendant attacks the testimony of the two representatives of the Ontario Government on the ground that—

“their investigation had covered a period of little more than a year, an exceedingly short time for scientific investigations such as we are here concerned with.”

In condemning an investigation as incomplete because it took “little more than a year” defendant might pause to consider that all of the animal tests upon which it relies were completed in a matter of weeks.

Defendant also attacks the testimony of the Ontario Government representatives on the ground that much of their investigation constituted a review of records and that these records were for the most part prepared by the parties involved herein. This is quite unsupported by, and at variance with, the record. First of all, the official investigators for the Ontario Government personally examined many patients under treatment at the Hendry Connell Research Foundation. (App. 56) Secondly, the case histories and reports which they examined were prepared by independent physicians who were for the most part unknown to the inventor. (App. 24, 35)

The record shows that from 600 to 1000 physicians used over 400,000 cubic centimeters of the product in issue in the treatment of their cancer patients. The reports of these physicians were forwarded to the Hendry Connell Research Foundation and examined in conjunction with other evidence by the representatives of the Ontario Government. (App. 34-35) In addition these investigators independently tested the value of this product at the Ontario Government Building. (App. 65)

Defendant, on page 7 of its brief, makes a special attack on Dr. Johns, one of the Ontario Government representatives, for "an unscientific ignoring of evidence which is adverse to that which it is desired to believe." Dr. Johns did not ignore the evidence relied on by defendant. On the contrary, he considered it very carefully and discarded it because it was palpably unsound and was based upon defective assumptions. Dr. Johns described in detail his reasons for rejecting this evidence. (App. 67-70) Defendant must have been satisfied with these reasons as Dr. Johns was not cross-examined thereon.

The testimony of the fifth and last witness, Dr. Robert N. Irwin, is attacked by defendant on the ground that he "has handled a very small number of cases and his study does not appear to have been sufficiently extensive to constitute a basis for holding the product useful." (Def. brief p. 7) Dr. Irwin became familiar with this invention in 1935 when he attended clinics at the General Hospital in Kingston where it was first used. In 1937 he administered this product at the Toronto General Hospital. Since that time he has used it on fourteen cancer patients. (App. 79-80) He is far better qualified than the laymen and laboratory scientists upon whom defendant must rest its case. Their total knowledge about this product was derived from a single, brief publication by Dr. Connell in the year 1935.

DEFENDANT'S CRITICISM OF THE DOCUMENTARY EVIDENCE.

Defendant states that plaintiff's documentary exhibits are self-serving, of little value, fragmentary, inconsistent and are not confined to pain reduction. (Def. brief pp. 8, 9)

As previously mentioned herein these exhibits are for the most part based upon the reports of hundreds of physicians throughout the civilized world. (App. 24, 35) The documentary exhibits are a fair and complete description of these cases. If defendant had any criticism of these

exhibits or the manner in which they were prepared he was free to cross-examine the witnesses who testified thereon. His failure to do so is significant.

These exhibits describe several hundred cases wherein pronounced pain relief was obtained with this product. Exhibit 3 shows that of eighty-three advanced cases treated with this product sixty-three evidenced improvement. Exhibit 4 shows that of two hundred and eighty-nine cases treated, which formerly required drugs for the relief of pain, two hundred and seventy-nine (96%) received partial or complete pain relief. Exhibit 7 shows that of fifty-nine cases of rectal cancer treated with this product forty-three cases received pain relief and symptomatic improvement. Exhibit 8 shows that one hundred and fifty-two cases in an advanced stage of cancer experienced partial or complete relief of pain with this product.

The documentary exhibits clearly demonstrate that the overwhelming number of patients treated with this product receive marked relief from pain.

Defendant criticizes certain of the case histories because they fail to mention pain relief. This omission is not surprising, however, as a small number of cancer patients are free from pain until the very end. (App. 57) Their case histories would obviously not refer to pain relief.

Defendant criticizes some of the case histories because they refer to certain advantages in addition to pain relief. It would be a strange and illogical rule which would penalize an invention for being better than presented, but that is evidently what defendant contends. The unsoundness of this contention is self-evident.

The inconsistency to which defendant refers on page 7 of its brief is actually non-existent. Treatment of the patient in question had been discontinued in July 1935 and never resumed. For several months the patient was completely free of pain, but thereafter it returned. This is not at all surprising as the patient had been without treatment for some months and had received but a brief series of injections prior thereto. Even under such unfavorable con-

ditions the patient experienced temporary relief and this is better than none at all.

Defendant asserts that since tumors sometimes regress spontaneously and since in certain cases regression of the tumor may produce pain relief a portion of the reports should be disregarded. (Def. brief p. 8) This assertion is unsound for two reasons; one, the instances of spontaneous regression are practically medical curiosities because of their rarity (App. 77); and two, tumor regression cannot explain many cases of pain reduction (App. 62, 71).

DEFENDANT'S EVIDENCE IS IRRELEVANT.

The most significant statement in defendant's brief occurs on page 10:

"It is stated first that the work of these experimenters (those relied on by defendant) *did not deal with pain relief* since animal experimentation does not indicate whether pain was being relieved or not. *This is true*, but inasmuch as all the case histories are so interbound not only with pain relief but also with recession of the tumor, change in tumor growth, and other symptomatic improvements, it is submitted that other work which reveals that such symptomatic improvements and change and recession of the tumor growth are not present is directly contradictory to the testimony adduced by appellant and clearly indicates the lack of utility of the product." (Parenthetical clause and italics ours.)

This goes to the very heart of the case. Since the sole issue is utility as to pain relief defendant's admission of absence of any evidence which negatives pain relief is worthy of note.

The second sentence of the foregoing excerpt endeavors to rectify this omission by the creation of a most unusual theory. As plaintiff understands this theory, it is to the effect that since some of plaintiff's evidence describes advantages of the product in issue in addition to pain reduction any evidence which disputes such Other Advantages negatives pain reduction.

This proposition is so ridiculous that defendant must have been desperate indeed to invoke it. Its acceptance would make the measure of utility depend on any and all extraneous advantages of a product.

The truth of the matter is that defendant's evidence should be disregarded in toto because:—

1. It relates only to animal experiments which cannot be used to evaluate pain reduction. (App. 26-28, 58, 67)
2. It relates only to tumor growth and is not concerned with pain reduction. (Def. brief pp. 8-10)
3. It is too brief and incomplete to justify any conclusion. (App. 27, 68)

Not only is defendant's evidence subject to the defects just referred to but it is also unreliable even as to the feature of tumor regression because of a further shortcoming. It is all based on a study of Transplantable Tumors whereas human beings are Never subjected to this type of cancer. (App. 70) This defect is also referred to in the paper by Ettinger upon which defendant relies:—

“The transplantable type of cancer is widely used for investigation, but, is open to the objection that it may not conform to life processes of human cancer, since the latter is invariably spontaneous and not judged transplantable.” (App. 169)

DEFENDANT DOES NOT DENY THAT THE PLEADINGS ADMIT UTILITY.

The sole issue in this case, utility, stands admitted by the pleadings. Plaintiff has referred to this in its main brief and defendant does not deny it.

Defendant endeavors to avoid the consequences of these pleaded admissions by contending that “utility must be established by convincing proof.” Defendant refers to several decisions, on pages 4 and 5 of its brief, which are supposed to support this proposition. These decisions do

not change the law on utility one iota from that set forth on pages 12 and 13 of plaintiff's main brief. Furthermore, they could not change this law because it was established by the United States Supreme Court and all of defendant's decisions are by courts subordinate thereto.

An examination of the four decisions cited by defendant shows that they are quite consistent with the decisions relied on by plaintiff. In fact, the case of *In re Oberweger* which is relied on most strongly by defendant refers with approval to one of the decisions mentioned in plaintiff's main brief (*Lamb Knit Goods Co. v. Lamb Glove & Mitten Co. et al*) wherein it was held that "a small degree of utility is sufficient to support a patent." 115 Fed. (2d) 826, 828.

In each of these decisions there was ample evidence to negative utility and little or no evidence in support thereof. It appears that in not a single case was there even an isolated instance of the invention producing a useful result however slight. Upon such records the courts properly held that the inventions lacked utility.

The record of the case at bar is replete with hundreds of cases of pronounced improvement. On the other hand defendant's evidence in this case is no better than that which the courts ignored in the foregoing decisions. An interesting parallel may be obtained from the *Hoover* case where the evidence was criticized and discarded because it did not represent the invention under actual operating conditions. This criticism is applicable to all of defendant's evidence, but to none of plaintiff's evidence.

Contrary to the contentions of defendant, the Supreme Court has consistently held that an invention possesses utility if it will accomplish its stated objective at all, even though it may be crude and imperfect. (Plaintiff's main brief p. 12) The invention need not be a commercial success and may be no better than the prior art. Nevertheless, if it accomplishes its desired objective TO ANY EXTENT WHATSOEVER it possesses "utility" as that term is used in the patent law. Since appellant's product

produces relief of pain in 65 per cent of the cases treated, the conclusion is inescapable that it possesses utility in a superlative degree.

MISCELLANEOUS.

Defendant admits that other governmental agencies than the Patent Office are charged with the duty of protecting the public in the case of drugs and medicinal products, but it contends:—

“However, rightly or wrongly, the public considers that when a device is patented it has been approved by the government, and the mere patenting of the device has *an advertising value* in and of itself which leads the public to place reliance thereon and to entertain hopes which may never be fulfilled.” (Def. brief p. 12) (*Italics ours*)

As pointed out in plaintiff's main brief, pp. 25 and 26, the present invention is of a type which is subjected to the most stringent regulations by the United States Public Health Service. This product cannot be sold or offered for sale until its efficacy and its method of production is approved by the United States Public Health Service and certified by the Secretary of the Treasury. Issuance of a patent, therefore, can have no advertising value until the product has received Government approval for sale. Furthermore, it should be borne in mind that this product is distributed only to physicians. The worries of defendant with respect to this feature of the invention, as in the case of many of his other arguments, are groundless and quite unsupported by either the record or common sense.

Plaintiff agrees with the defendant that “the progress of science and the useful arts is not promoted by an indiscriminate granting of patents on medicinal preparations of doubtful value.” However, this does not apply to the present invention as its value has been demonstrated over a period of more than five years by hundreds of independent physicians on more than a thousand patients in the

last stages of cancer. Any more convincing evidence of utility is hard to imagine. In fact, *one might ask just what proof the defendant would consider sufficient.* It is believed to be a conservative statement that the Patent Office has never before been presented with such complete and conclusive evidence in support of the utility of any invention.

Defendant admits that the need of the medical practitioner for a product which would alleviate pain in cases of cancer is great, but contends that this is irrelevant. It is submitted that it is not as irrelevant as it might superficially appear. The great and admitted need for a pain alleviant for cancer is conclusive proof of the complexity of this problem. Cancer is one of the first diseases referred to in the records of medical science. It is the disease which has baffled the most brilliant minds of the medical profession. The main problem of cancer is to prevent it or cure it but pain alleviation is a problem of vital importance, as conceded by the defendant.

Since there is no other satisfactory pain alleviant for cancer it is clear that this product was critically evaluated by the many hundreds of physicians who have used it. Their testimony and reports thereon should therefore be given great weight.

On page 2 of its brief defendant criticizes plaintiff for stating that:

“The District Court has found as a fact that the testimony of plaintiff’s witnesses and certain of the exhibits was to the effect that the invention had reduced pain due to cancer in approximately 65 per cent of the cancer patients treated therewith.”

This statement is accurate and complete. It is taken verbatim from the Findings of Fact. (App. 179, 180) The remainder of the finding does not in any way qualify this quotation or impair its effectiveness, for it refers merely to “negative tests” reported in papers relied on by the

defendant. These papers—as admitted by defendant—DO NOT DEAL WITH PAIN RELIEF. (Def. brief p. 10)

Actually, therefore, plaintiff was most circumspect in using this quotation. Instead of referring only to what plaintiff's witnesses and exhibits proved he might truthfully have stated that:

ALL THE EVIDENCE IN THIS CASE DEALING WITH THE QUESTION OF PAIN REDUCTION PROVES THAT 65 PER CENT OF THE CANCER PATIENTS TREATED OBTAINED PAIN RELIEF.

CONCLUSION.

It is respectfully and urgently submitted that there exists neither rational nor statutory basis for the conclusions reached by the Patent Office and the District Court. It is accordingly prayed that the decree of the District Court should be reversed and the Commissioner of Patents authorized to issue a patent on this invention which is one of the few meritorious contributions to a field which is in crying need of assistance.

Respectfully submitted,

ARTHUR G. CONNOLLY,
JAMES P. BURNS,
Counsel for Plaintiff-Appellant.

